Complete listing of claims:

- 1. (Withdrawn) A pharmaceutical composition comprising a corticotropin releasing factor antagonist and a growth hormone secretagogue or growth hormone.
- 2. (Withdrawn) A pharmaceutical composition according to claim 1 wherein said corticotropin releasing factor antagonist is a compound of formula

or a pharmaceutically acceptable acid addition salt thereof, wherein A is NR_1R_2 , $CR_1R_2R_{11}$, or $C(=CR_1R_{12})R_2$, $NHCR_1R_2R_{11}$, $OCR_1R_2R_{11}$, $SCR_1R_2R_{11}$, $NHNR_1R_2$, $CR_2R_{11}NHR_1$, $CR_2R_{11}OR_1$, $CR_2R_{11}SR_1$ or $C(O)R_2$;

 R_1 is hydrogen, or C_1 - C_6 alkyl which may be substituted by one or two substituents R_6 independently selected from the group consisting of hydroxy, fluoro, chloro, bromo, iodo, C_1 - C_6 alkoxy, O-C(O)-(C_1 - C_6 alkyl), O-C(O)-N(C_1 - C_4 alkyl)(C_1 - C_2 alkyl); amino, NH(C_1 - C_4 alkyl), S(C_1 - C_6 alkyl), OC(O)NH(C_1 - C_4 alkyl), N(C_1 - C_2 alkyl)C(O)(C_1 - C_4 alkyl), NHC(O)(C_1 - C_4 alkyl), COOH, CO(C_1 - C_4 alkyl), C(O)NH(C_1 - C_4 alkyl), C(O)N(C_1 - C_4 alkyl)(C_1 - C_2 alkyl), SH, CN, NO₂, SO(C_1 - C_4 alkyl); SO₂NH(C_1 - C_4 alkyl), SO₂N(C_1 - C_4 alkyl)(C_1 - C_2 alkyl), and said C_1 - C_6 alkyl may have one or two double or triple bonds;

R₂ is C₁-C₁₂ alkyl, aryl or (C₁- C₁₀alkylene)aryl wherein said aryl is phenyl, naphthyl, thienyl, benzothienyl, pyridyl, quinolyl, pyrazinolyl, pyrimidyl, imidazolyl, furanyl, benzofuranyl, benzothiazolyl, isothiazolyl, benzisothiazolyl, thiazolyl, isoxazolyl, benzisoxazolyl, benzimidazolyl, triazolyl, pyrazolyl, pyrrolyl, indolyl, azaindolyl, oxazolyl, or benzoxazolyl; 3- to 8-membered cycloalkyl or (C₁-C₆ alkylene) cycloalkyl, wherein said cycloalkyl may have one or two of O, S or N-Z, wherein Z is hydrogen, substituted, independently, for one or two carbons of said cycloalkyl, C1-C4 alkyl, benzyl or C1-C4 alkanoyl, wherein R² may be substituted independently by from one to three of chloro, fluoro, or C₁-C₄ alkyl, or one of hydroxy, bromo, iodo, C₁-C6 alkoxy, OC(O)(C₁-C6 alkyl), O-C-N(C₁-C4 alkyl)(C₁-C2 alkyl), $S(C_1-C_6)$ alkyl), NH_2 , $NH(C_1-C_2)$ alkyl), $N(C_1-C_4)$ alkyl), $C(O)(C_1-C_4)$ alkyl), $C(O)(C_1-C_4)$ COOH, C(O)O(C_1 - C_4 alkyl), C(O)NH(C_1 - C_4 alkyl), C(O)N(C_1 - C_4 alkyl)(C_1 - C_2 alkyl), SH, CN, NO₂, $SO(C_1-C_4 \text{ alkyl})$, $SO_2(C_1-C_4 \text{ alkyl})$, $SO_2NH(C_1-C_4 \text{ alkyl})$, $SO_2N(C_1-C_4 \text{ alkyl})$ ($C_1-C_2 \text{ alkyl}$), and wherein said C_1 - C_{12} alkyl or C_1 - C_{10} alkylene may have one to three double or triple bonds; or NR₁R₂ or CR₁R₂R₁₁ may form a 4- to 8-membered ring optionally having one or two double bonds or one or two of O, S or N-Z wherein Z is hydrogen, C₁-C₄ alkyl, benzyl, or C₁-C₄ alkanoyl; R₃ is hydrogen, C₁-C₆ alkyl, fluoro, chloro, bromo, iodo, hydroxy, amino, O(C₁-C₆ alkyl), NH(C₁-C₆ alkyl), $N(C_1-C_4 \text{ alkyl})(C_1-C_2 \text{ alkyl})$, SH, $S(C_1-C_4 \text{ alkyl})$, $SO(C_1-C_4 \text{ alkyl})$, or $SO_2(C_1-C_4 \text{ alkyl})$, wherein said C₁-C₄ alkyl and C₁-C₆ alkyl may have one or two double or triple bonds and may be substituted -4-USERS\DOCS\LA21952\LPAED\4k9y01!.DOC / 212902

by from 1 to 3 R, substituents independently selected from the group consisting of hydroxy, amino, C₁-C₃ alkoxy, dimethylamino, diethylamino, methylamino, ethylamino, NHC(O)CH₃, fluoro, chloro or C₁-C₃ thioalkyl;

 R_4 is hydrogen, C_1 - C_6 alkyl, fluoro, chloro, bromo, iodo, C_1 - C_6 alkoxy, amino, NH(C_1 - C_6 alkyl), N(C_1 - C_6 alkyl), SO_n(C_1 - C_6 alkyl), wherein n is O, 1 or 2, cyano, hydroxy, carboxy, or amido, wherein said C_1 - C_6 alkyls may be substituted by one to three of hydroxy, amino, carboxy, amido, NHC(O)(C_1 - C_4 alkyl), NH(C_1 - C_4 alkyl), N(C_1 - C_4 alkyl), C(O)O(C_1 - C_4 alkyl), C(O)O(C_1 - C_4 alkyl), C₁- C_3 thioalkyl, fluoro, bromo, chloro, iodo, cyano or nitro;

 R_5 is phenyl, naphthyl, thienyl, benzothienyl, pyridyl, quinolyl, pyrazinolyl, pyrimidyl, imidazolyl, furanyl, benzofuranyl, benzothiazolyl, isothiazolyl, benzoisothiazolyl, thiazolyl, isoxazolyl, benzisoxazolyl, benzisoxazolyl, benzisoxazolyl, pyrrolidinyl, benzimidazolyl, triazolyl, pyrrazolyl, pyrrolyl, indolyl, pyrrolopyridyl benzoxazolyl, oxazolyl, pyrrolidinyl, thiazolidinyl, piperazinyl, piperidinyl, or tetrazolyl, wherein each one of the above groups may be substituted independently by from one to three of fluoro, chloro, bromo, formyl, C_1 - C_6 alkyl, C_1 - C_6 alkoxy or trifluoromethyl, or one of hydroxy, iodo, cyano, nitro, amino, cyclopropyl, NH(C_1 - C_4 alkyl), N(C_1 - C_4 alkyl), COO(C_1 - C_4 alkyl), CO(C_1 - C_4 alkyl), SO₂NH(C_1 - C_4 alkyl), SO₂NH(C_1 - C_4 alkyl), SO₂NH₂, NHSO₂(C_1 - C_4 alkyl), S(C_1 - C_6 alkyl), SO₂(C_1 - C_6 alkyl), wherein said C_1 - C_4 alkyl and C_1 - C_6 alkyl may have one double or triple bond and may be substituted by one or two of fluoro, chloro, hydroxy, amino, methylamino, dimethylamino or acetyl; with the proviso that R_5 is not unsubstituted phenyl;

 R_{11} is hydrogen, hydroxy, fluoro, chloro, COO(C_1 - C_2 alkyl), cyano, or CO(C_1 - C_2 alkyl); and R_{12} is hydrogen or C_1 - C_4 alkyl; with the provisos that:

- (a) A is not straight chain C₁-C₁₂ alkyl;
- (b) when R_3 is hydrogen, A is benzyl or phenethyl, and R_4 is fluoro, chloro, bromo or iodo, then R_5 is not 5'-deoxy-ribofuranosyl or 5'-amino-5'-deoxy-ribofuranosyl; and
 - (c) when R⁵ is phenyl, said phenyl is substituted by two or three substituents.
- 3. (Withdrawn) A pharmaceutical composition according to claim 1 wherein said corticotropin releasing factor antagonist is a compound of formula B

$$R_3$$
 R_4
 R_5
 R_4
 R_6

and the pharmaceutically acceptable acid addition salts thereof, wherein

B is NR_1R_2 , $CR_1R_2R_{11}$, $C(=CR_2R_{12})R_1$, $NHR_1R_2R_{11}$, $OCR_1R_2R_{11}$, $SCR_1R_2R_{11}$, $NHNR_1R_2$, $CR_2R_{11}NHR_1$, $CR_2R_{11}OR_1$, $CR_2R_{11}SR_1$, or $C(O)R_2$;

 R_1 is hydrogen, or C_1 - C_6 alkyl which may be substituted by one or two substituents R_7 independently selected from the group consisting of hydroxy, fluoro, chloro, bromo, iodo, C_1 - C_8 alkoxy, O-C(=O)- C_1 - C_6 alkyl), O-C(=O)NH(C_1 - C_4 alkyl), O-C(=O)-N(C_1 - C_4 alkyl)(C_1 - C_2 alkyl), amino, NH(C_1 - C_4 alkyl), N(C_1 -USERSNDOCS\(\text{LA21952\(\text{LPAED\(\text{MSY}\(\text{DOC}\)\)})=5-

 $C_2 \text{ alkyl})(C_1-C_4 \text{ alkyl}), \ S(C_1-C_6 \text{ alkyl}), \ N(C_1-C_4 \text{ alkyl})C(=O)(C_1-C_4 \text{ alkyl}), \ NH(C_1-C_4 \text{ alkyl}), \ COOH, \\ C(=O)O(C_1-C_4 \text{ alkyl}), \ C(=O)NH(C_1-C_4 \text{ alkyl}), \ C(=O)N(C_1-C_4 \text{ alkyl})(C_1-C_2 \text{ alkyl}), \ SH, \ CN, \ NO_2, \ SO(C_1-C_4 \text{ alkyl}), \ SO_2(C_1-C_4 \text{ alkyl}), \ SO_2NH(C_1-C_4 \text{ alkyl}), \ SO_2N(C_1-C_4 \text{ alkyl}), \ and \ said \ C_1-C_6 \text{ alkyl}) \\ may contain one or two double or triple bonds;$

 R_2 is C_1 - C_{12} alkyl, aryl or $(C_1$ - C_{10} alkylene)aryl wherein said aryl is phenyl, naphthyl, thienyl, benzothienyl, pyridyl, quinolyl, pyrazinyl, pyrimidyl, imidazolyl, furanyl, benzofuranyl, benzothiazolyl, isothiazolyl, benzisothiazolyl, thiazolyl, isoxazolyl, benzisoxazolyl, benzimidazolyl, triazolyl, pyrrolyl, indolyl, pyrrolopyridyl, oxazolyl, or benzoxazolyl; 3- to 8-membered cycloalkyl or $(C_1$ - C_6 alkylene) cycloalkyl, wherein said cycloalkyl may contain one or two of O, S or N-Z wherein Z is hydrogen, C_1 - C_4 alkyl, benzyl or C_1 - C_4 alkanoyl, wherein R_2 may be substituted independently by from one to three of chloro, fluoro, or C_1 - C_4 alkyl, or one of hydroxy, bromo, iodo, C_1 - C_6 alkoxy, O-C(=O)- $(C_1$ - C_6 alkyl), O-C- $N(C_1$ - C_4 alkyl)(C_1 - C_2 alkyl), $N(C_1$ - C_6 alkyl), $N(C_1$ - C_4 alkyl), $N(C_1$ - $N(C_$

 R_3 is hydrogen, C_1 - C_6 alkyl, fluoro, chloro, bromo, iodo, hydroxy, amino, $O(C_1$ - C_6 alkyl), $NH(C_1$ - C_6 alkyl), $N(C_1$ - C_4 alkyl)(C_1 - C_2 alkyl), SH, $S(C_1$ - C_4 alkyl), $SO(C_1$ - C_4 alkyl), or $SO_2(C_1$ - C_4 alkyl), wherein said C_1 - C_4 alkyl and C_1 - C_6 alkyl may contain from one or two double or triple bonds and may be substituted by from 1 to 3 substituents R8 independently selected from the group consisting of hydroxy, amino, C_1 - C_3 alkoxy, dimethylamino, methylamino, methylamino, ethylamino, NHCH₃, fluoro, chloro or C_1 - C_3 thioalkyl;

 R_4 and R_6 are each independently hydrogen, C_1 - C_6 alkyl, fluoro, chloro, bromo, iodo, C_1 - C_6 alkoxy, amino, NH(C_1 - C_6 alkyl), N(C_1 - C_6 alkyl)(C_1 - C_2 alkyl), SO_n(C_1 - C_6 alkyl), wherein n is O, 1 or 2, cyano, hydroxy, carboxy, or amido, wherein said C_1 - C_6 alkyls may be substituted by one to three of hydroxy, amino, carboxy, amido, NHC(=O)(C_1 - C_4 alkyl), NH(C_1 - C_4 alkyl), N(C_1 - C_4 alkyl), C(=O)O(C_1 -C4 alkyl), C_1 - C_3 alkoxy, C_1 - C_3 thioalkyl, fluoro, bromo, chloro, iodo, cyano or nitro;

 R_5 is phenyl, naphthyl, thienyl, benzothienyl, pyridyl, quinolyl, pyrazinyl, pyrimidyl, imidazolyl, furanyl, benzofuranyl, benzothiazolyl, isothiazolyl, benzisothiazolyl, thiazolyl, isoxazolyl, benzisoxazolyl, benzimidazolyl, triazolyl, pyrazolyl, pyrrolyl, indolyl, azaindolyl, benzoxazolyl, oxazolyl, pyrrolidinyl, thiazolidinyl, morpholinyl, piperidinyl, piperazinyl, tetrazolyl, or 3- to 8-membered cycloalkyl or 9- to 12-membered bicycloalkyl, optionally containing one to three of O, S or N-Z wherein Z is hydrogen, C_1 - C_4 alkyl, C_1 - C_4 alkanoyl, phenyl or phenylmethyl, wherein each one of the above groups may be substituted independently by from one to four of fluoro, chloro, C_1 - C_6

alkyl, C_1 - C_6 alkoxy or trifluoromethyl, or one of bromo, iodo, cyano, nitro, amino, NH(C_1 - C_4 alkyl), N(C_1 - C_4 alkyl), CO(C_1 - C_4 alkyl), CO(C_1 - C_4 alkyl), SO₂NH(C_1 - C_4 alkyl), SO₂NH(C_1 - C_4 alkyl), SO₂NH₂, NHSO₂(C_1 - C_4 alkyl), S(C_1 - C_6 alkyl), SO₂(C_1 - C_6 alkyl), wherein said C_1 - C_4 alkyl and C_1 - C_6 alkyl may be substituted by one or two of fluoro, chloro, hydroxy, amino, methylamino, dimethylamino or acetyl; with the proviso that R₅ is not unsubstituted phenyl;

 R_{11} is hydrogen, hydroxy, fluoro, chloro, COO(C_1 - C_2 alkyl), cyano, or CO(C_1 - C_2 alkyl); and R_{12} is hydrogen or C_1 - C_4 alkyl; with the proviso that (1) when R_5 is 4-bromophenyl, R_3 is hydrogen, and R_4 and R_6 are methyl, then B is not methylamino or ethyl, and (2) when R_5 is 4-bromophenyl, and R_3 , R_4 and R_6 are methyl, then B is not 2-hydroxyethylamino.

4. (Currently amended) A pharmaceutical composition <u>comprising a corticotropin releasing</u> <u>factor antagonist and a growth hormone secretagogue or growth hormone</u>, according to claim 1 wherein said corticotropin releasing factor antagonist is a compound of formula

wherein

A is CR₇ or N;

B is NR_1R_2 , $CR_1R_2R_{11}$, $C(=CR_2R_{12})R_1$, $NHCHR_1R_2$, $OCHR_1R_2$, $SCHR_1R_2$, CHR_2OR_{12} , CHR_2SR_{12} , $C(S)R_2$ or $C(O)R_2$;

G-is-oxygen, sulfur, NH, NH₃, hydrogen, methoxy, ethoxy, trifluoromethoxy, methyl, ethyl, thiomethoxy, NH₂, NHCH₃, N(CH₃)₂ or trifluromethyl;

Y is CH or N;

 R_2 is C_1 - C_{12} alkyl, aryl or (C_1 - C_4 alkylene)aryl wherein said aryl is phenyl, naphthyl, thienyl, benzothienyl, pyridyl, quinolyl, pyrazinyl, pyrimidyl, imidazolyl, furanyl, benzothiazolyl, usersydocsylazi952ylpaedylgyoii.doc/212902 - 7 -

isothiazolyl, benzisothiazolyl, benzisoxazolyl, benzimidazolyl, indolyl, or benzoxazolyl; 3- to 8-membered cycloalkyl or $(C_1-C_6$ alkylene)cycloalkyl, wherein said cycloalkyl may contain one or two of O, S or N-R₉ wherein R₉ is hydrogen, or C₁-C₄ alkyl, wherein the above defined R₂ may be substituted independently by from one to three of chloro, fluoro, or C₁-C₄ alkyl, or one of bromo, iodo, C₁-C₆ alkoxy, O-CO-(C₁-C₆ alkyl), O-CO-N(C₁-C₄ alkyl)(C₁-C₂ alkyl), S(C₁-C₆ alkyl), CN, NO₂, SO(C₁-C₄ alkyl), or SO₂(C₁-C₄ alkyl), and wherein said C₁-C₁₂ alkyl or C₁-C₄ alkylene may contain one double or triple bond; or

 NR_1R_2 or $CR_1R_2R_{11}$ may form a saturated 5- to 8-membered carbocyclic ring which may contain one or two double bonds or one or two of O or S;

R₃ is methyl, ethyl, fluoro, chloro, bromo, iodo, cyano, methoxy, OCF₃, methylthio, methylsulfonyl, CH₂OH or CH₂OCH₃;

 R_4 is hydrogen, C_1 - C_4 alkyl, fluoro, chloro, bromo, iodo, C_1 - C_4 alkoxy, amino, nitro, NH(C_1 - C_4 alkyl), N(C_1 - C_4 alkyl)(C_1 - C_2 alkyl), SO_n(C_1 - C_4 alkyl), wherein n is O, 1 or 2, cyano, hydroxy, CO(C_1 - C_4 alkyl), CHO, or COO(C_1 - C_4 alkyl), wherein said C_1 - C_4 alkyl may contain one or two double or triple bonds and may be substituted by one or two of hydroxy, amino, carboxy, NHCOCH₃, NH(C_1 - C_2 alkyl), N(C_1 - C_2 alkyl)₂, COO(C_1 - C_4 alkyl), CO(C_1 - C_4 alkyl), C_1 - C_3 alkoxy, C_1 - C_3 thioalkyl, fluoro, chloro, cyano or nitro;

 R_5 is phenyl, naphthyl, thienyl, benzothienyl, pyridyl, quinolyl, pyrazinyl, pyrimidyl, furanyl, benzofuranyl, benzothiazolyl, or indolyl, wherein each one of the above groups R_5 is substituted independently by from one to three of fluoro, chloro, C_1 - C_6 alkyl, or C_1 - C_6 alkoxy, or one of hydroxy, iodo, bromo, formyl, cyano, nitro, trifluoromethyl, amino, NH(C_1 - C_4 alkyl), N(C_1 - C_6)(C_1 - C_2 alkyl), COH, COO(C_1 - C_4 alkyl), CO(C_1 - C_4 alkyl), SO₂NH(C_1 - C_4 alkyl), SO₂NH(C_1 - C_4 alkyl), SO₂NH₂, NHSO₂(C_1 - C_4 alkyl), S(C_1 - C_6 alkyl), or SO₂(C_1 - C_6 alkyl), wherein said C_1 - C_4 alkyl and C_1 - C_6 alkyl may be substituted by one or two of fluoro, hydroxy, amino, methylamino, dimethylamino or acetyl;

 R_6 is hydrogen, or C_4 - C_6 -alkyl, wherein said C_4 - C_6 -alkyl may be substituted by one hydroxy, methoxy, ethoxy or fluoro;

 R_7 is hydrogen, C_1 - C_4 alkyl, fluoro, chloro, bromo, iodo, cyano, hydroxy, $O(C_1$ - C_4 alkyl), $C(O)(C_1$ - C_4 alkyl), or $C(O)O(C_1$ - C_4 alkyl), wherein the C_1 - C_4 alkyl groups may be substituted with one hydroxy, chloro or bromo, or one to three fluoro;

R¹¹ is hydrogen, hydroxy, fluoro, or methoxy;

R¹² is hydrogen or C₁-C₄ alkyl; and

R₁₆ and R₁₇ are each independently hydrogen, hydroxy, methyl, ethyl, methoxy, or ethoxy, except that they are not both methoxy or ethoxy, and CR₄R₆ and CR1₆R₁₇ each independently may be C=O

wherein said growth hormone secretagogue is a compound of formula IV:

HET
$$R^4$$
 R^6 R^7 R^8 R^6 R^8

or a stereoisomeric mixture thereof, a diastereomerically enriched, diastereomerically pure, enantiomerically enriched, or enantiomerically pure isomer thereof, or a prodrug of such compound, mixture, or isomer thereof, or a pharmaceutically acceptable salt of the compound, mixture, isomer, or prodrug, wherein in formula IV:

HET is a heterocyclic moiety selected from the group consisting of

$$\begin{array}{c} & & & \\$$

d is 0, 1, or 2;

e is 1 or 2;

f is 0 or 1;

n and w are 0, 1, or 2, provided that n and w cannot both be O at the same time; Y^2 is oxygen or sulfur;

A is a divalent radical, wherein the left hand side of the radical as shown below is connected to C" and the right hand side of the radical as shown below is connected C', selected from the group consisting of -NR²-CO-NR²-, -NR ²-SO₂-NR²-, -O-CO-NR²-, -NR²-CO₂-, -CO-NR²-CO-, -CO-NR²-C(R⁹R¹⁰O)-, -C(R9R10)-NR2-CO-,-C(R9R10)-C(R9R10)-C(R9R10)-, -SO2-C(R9R10)-C(R9R $C(R^9R^{10})$ -O- $C(R^9R^{10})$ -, -NR²-CO- $C(R^9R^{10})$ -, -O-CO- $C(R^9R^{10})$ -, -C(R⁹R¹⁰)-CO-NR²-, -CO-NR²-CO-, -C(R⁹R¹⁰)-CO₂-, -CO-NR²-C(R⁹R¹⁰)-C(R⁹R¹⁰)-CO₂-C(R⁹R¹⁰)-, -C(R⁹R¹⁰)-C(R⁹R¹⁰)-C(R⁹R¹⁰)-C(R⁹R¹⁰)-, -C(R⁹R¹⁰)-C(R⁹R¹⁰)-, -C(R⁹R¹⁰)-C(R⁹R¹⁰)-, -C(R⁹R¹⁰)-, SO₂-NR²-C(R⁹R¹⁰)-C(R⁹R¹⁰)-, -C(R⁹R¹⁰)-C(R⁹R¹⁰)-NR²-CO-, -C(R⁹R¹⁰)-C(R⁹R¹⁰)-O-CO-, -NR²-CO-<u>C(R⁹R¹⁰)-C(R⁹R¹⁰)--NR²-SO₂-C(R⁹R¹⁰)-C(R⁹R¹⁰)--O-CO-C(R⁹R¹⁰)-C(R⁹R^{10</u>} NR^2 -, $-C(R^9R^{10})-C(R^9R^{10})-CO$ - $-C(R^9R^{10})-NR^2-CO_2-C(R^9R^{10})-O-CO-NR^2$, $-C(R^9R^{10})-NR^2-CO-NR^2$ -, $-C(R^9R^{10})-C(R^9R^{1$ $NR^2-CO_2-C(R^9R^{10})-$, $-NR^2-CO-NR^2-C(R^9R^{10})-$, $-NR^2-SO_2-NR^2-C(R^9R^{10})-$, $-O-CO-NR^2-C(R^9R^{10})-$, $-O-CO-NR^2-C(R^9R^{10}) CO-N=C(R^{11})-NR^2-$, $-CO-NR^2-C(R^{11})=N-$, $-C(R^9R^{10})-NR^{12}-C(R^9R^{10})-$, $-NR^{12}-C(R^9R^{10})-$, $-NR^{12}-C(R^9R^{10}) C(R^9R^{10})-C(R^9R^{10})-C(R^9R^{10})-C(R^9R^{10})-C(R^1R^{10})-C(R^1R^{10})-C(R^1R^{10})-C(R^9R^{10})-C(R^{10})-C(R^{10})-C(R^{10})-C(R^{10})-C(R^{10})-C(R^{10})-C(R^{10}$ $-C(R^9R^{10})-NR^{12}-, -N=C(R^{11})-NR^2-CO-, -C(R^9R^{10})-C(R^9R^{10})-NR^2-SO_2-, -C(R^9R^{10})-C(R^9R^{10})-SO_2 NR^2$ -, $-C(R^9R^{10})-C(R^9R^{10})-CO_2$ - $-C(R^9R^{10})-SO_2$ - $-C(R^9R^{10})-C(R^9R^{10})-C(R^9R^{10})$ $C(R^9R^{10})-C(R^9R^{10})-C(R^9R^{10})-C(R^9R^{10})-C$, $-C(R^9R^{10})-C$, $-C(R^9R^{10})-C$, $-C(R^9R^{10})-C$ and -C(R9R10)-NR2-SO2-NR2-;

Q is a covalent bond or CH2;

W is CH or N;

X is CR^9R^{10} , $C=CH_2$, or C=O;

Y is CR⁹R¹⁰, O, or NR²;

Z is C=O, C=S, or SO₂;

 G^1 is hydrogen, halo, hydroxy, nitro, amino, cyano, phenyl, carboxyl, -CONH₂, -C₁-C₄ alkyl optionally independently substituted with one or more phenyl, one or more halogen, or one or more hydroxy groups, -C₁-C₄ alkoxy optionally independently substituted with one or more phenyl, one or more halogen, or one or more hydroxy groups, -C₁-C₄ alkylthio, phenoxy, -CO₂-(C₁-C₄ alkyl), N,N-di-(C₁-C₄ alkylamino), -C₂-C₆ alkenyl optionally independently substituted with one or more phenyl, one or more halogen, or one or more hydroxy groups, -C₂-C₆ alkynyl optionally independently substituted with one or more phenyl, one or more halogen, or one or more hydroxy groups, -C₃-C₆ cycloalkyl optionally independently substituted with one or more C_1 -C₄ alkyl groups, one or more halogen, or one or more hydroxy groups, -C₁-C₄ alkylamino carbonyl, or di-C₁-C₄ alkylamino) carbonyl;

G2 and G³ are each independently selected from the group consisting of hydrogen, halo, hydroxy, $-C_1-C_4$ alkyl optionally independently substituted with one to three halo groups, and $-C_1-C_4$ alkoxy optionally independently substituted with one to three halo groups; R¹ is hydrogen, -CN, $-(CH_2)_qNX^6COX^6$, $-(CH_2)_qNX^6CO(CH_2)-A^1$, $-(CH_2)_qNX^6SO_2(CH_2)-A^1$, $-(CH_2)_qNX^6SO_2X^6$, $-(CH_2)_qNX^6CONX^6(CH_2)_t-A^1$, $-(CH_2)_qNX^6CONX^6X^6$, $-(CH_2)_qCONX^6X^6$, $-(CH_2)_qCONX^6X^6$, $-(CH_2)_qCOX^6$, $-(CH_2)_q$

 $\frac{(CH_2)_{q}CO(CH_2)_{t}-A^1, -(CH_2)_{q}NX^6CO_2X^6, -(CH_2)_{q}NX^6SO_2NX^6X^6, -(CH_2)_{q}SO_{m}X^6, -(CH_2)_{q}SO_{m}X^6, -(CH_2)_{q}SO_{m}(CH_2)_{t}-A^1, -C_1-C_{10}$

 $(CH_2)_g - Y^1 - (CH_2)_t - A^1$, or $-(CH_2)_g - Y^1 - (CH_2)_t - (C_3 - C_1 \text{ cycloalkyl})$;

wherein the alkyl and cycloalkyl groups in the definition of R^1 are optionally substituted with C_1 - C_4 alkyl, hydroxy, C_1 - C_4 alkoxy, carboxyl, - $CONH_2$, - SO_m - $(C_1$ - C_6 alkyl), - CO_2 - $(C_1$ - C_4 alkyl) ester, 1H-tetrazol-5-yl, or 1, 2, or 3 fluoro groups;

Y' is O, SO_m, -CONX⁶-, -CH=CH-, -C=C-, -NX⁶CO-, -CONX⁶-, -CO₂-, -OCONX⁶- or -OCO-; q is O, 1, 2, 3, or 4;

t is O, 1, 2, or 3;

said $(CH_2)_q$ group and $(CHA \text{ group in the definition of R' are optionally independently substituted with hydroxy, <math>C_1$ - C_4 alkoxy, carboxyl, $-CONH_2$, $-SO_m$ - $(C_1$ - C_6 alkyl), $-CO_2$ - $(C_1$ - C_4 alkyl) ester, 1 H-tetrazol-5-yl, 1, 2, or 3 fluoro groups, or 1 or 2 C_1 - C_4 alkyl groups;

 R^{1A} is selected from the group consisting of hydrogen, F, CI, Br, I, C_1 - C_6 alkyl, phenyl- $(C_1$ - C_3 alkyl), provided that R^{1A} is not F, CI, Br, or I when a heteroatom is vicinal to C";

 R^2 is hydrogen, C_1 - C_8 alkyl, -(C_0 - C_3 alkyl)-(C_3 - C_8 cycloalkyl), -(C_1 - C_4 alkyl)-A', or A', wherein the alkyl groups and the cycloalkyl groups in the definition of R^2 are optionally substituted with hydroxy, -CO2 R^6 , -CONX⁶X⁶, -NX⁶X⁶, -SO_m(R^6 , -SO_m(R^6 , -COA', -COA', -COX⁶, CF₃, CN, or 1, 2, or 3 independently selected halo groups;

 R^3 is selected from the group consisting of A', C_1 - C_{10} alkyl, -(C_1 - C_6 alkyl)-A', - (C_1 - C_6 alkyl)-(C_3 - C_1 cycloalkyl), -(C_1 - C_5 alkyl)-X'-(C_1 - C_5 alkyl)-X'-(C_1 - C_5 alkyl)-X'-(C_1 - C_5 alkyl)-X'-(C_1 - C_5 alkyl)-(C_3 - C_1 cycloalkyl);

wherein the alkyl groups in the definition of \mathbb{R}^3 are optionally substituted with $-SO_m(C_1-C_6 \text{ alkyl})$, $-CO2X^3$, 1, 2, 3, 4, or 5 independently selected halo groups, or 1, 2, or 3 independently selected $-OX^3$ groups;

X' is O, SO_{m_1} -NX²CO-, -CONX²-, -OCO-, -CO₂-, -CX²=CX²-, -NX²CO₂-, -OCONX²-, or -C²-. R⁴ is hydrogen, C_1 - C_6 alkyl, or C_3 - C_7 cycloalkyl, or R⁴ taken together with R³ and the carbon atom to which they are attached form C_5 - C_1 cycloalkyl, C_5 - C_1 cycloalkenyl, a partially saturated or fully saturated 4- to 8-membered ring having 1 to 4 heteroatoms independently selected from the group consisting of oxygen, sulfur, and nitrogen, or a bicyclic ring system consisting of a partially saturated or fully saturated 5- or 6-membered ring, fused to a partially saturated, fully unsaturated, or fully saturated 5- or 6-membered ring, optionally having 1 to 4 heteroatoms independently selected from the group consisting of nitrogen, sulfur, and oxygen;

 X^4 is hydrogen or C_1 - C_6 alkyl, or X^4 is taken together with R^4 and the nitrogen atom to which X^4 is attached and the carbon atom to which R^4 is attached and form a five to seven membered ring; R^6 is a bond or is

$$Z^{1}$$
 (CH₂)a (CH₂)b ;

wherein a and b are each independently O, 1, 2, or 3;

 X^5 and X5a are each independently selected from the group consisting of hydrogen, CF_3 , A', and C_1 - C_6 alkyl optionally substituted with A', OX^2 , - SO_1 - C_1 - C_6 alkyl), - CO_2 X2, C_3 - C_7 cycloalkyl, - NX^2X^2 , or - $CONX^2X^2$;

or the carbon bearing X⁵ or X^{5a} forms one or two alkylene bridges with the nitrogen atom bearing R⁷ and R⁸ wherein each alkylene bridge contains 1 to 5 carbon atoms, provided that when one alkylene bridge is formed then only one of X⁵ or X⁵a is on the carbon atom and only one of R⁷ or R⁸ is on the nitrogen atom, and further provided that when two alkylene bridges are formed then X⁵ and X^{5a} cannot be on the carbon atom and R⁷ and R⁸ cannot be on the nitrogen atom;

or X⁵ taken together with X ^{5a} and the carbon atom to which they are attached form a partially saturated or fully saturated 3- to 7-membered ring, or a partially saturated or fully saturated 4- to 8-membered ring having 1 to 4 heteroatoms independently selected from the group consisting of oxygen, sulfur, and nitrogen;

or X⁵ taken together with X^{5a} and the carbon atom to which they are attached form a bicyclic ring system consisting of a partially saturated or fully saturated 5- or 6-membered ring, optionally having 1 or 2 heteroatoms independently selected from the group consisting of nitrogen, sulfur, and 3O

oxygen, fused to a partially saturated, fully saturated, or fully unsaturated 5- or 6-membered ring, optionally having 1 to 4 heteroatoms independently selected from the group consisting of nitrogen, sulfur, and oxygen;

 $\underline{Z^1}$ is a bond, O, or N-X², provided that when a and b are both O then Z' is not N-X² or O; $\underline{R^7}$ and $\underline{R^8}$ are each independently hydrogen or $\underline{C_1}$ - $\underline{C_6}$ alkyl optionally independently substituted with $\underline{A'}$, $\underline{-CO_2}$ -($\underline{C_1}$ - $\underline{C_6}$ alkyl), $\underline{-SO_m}$ ($\underline{C_1}$ - $\underline{C_6}$ alkyl), 1 to 5 halo groups, 1 to 3 hydroxy groups, 1 to 3 -O-CO($\underline{C_1}$ - $\underline{C_{10}}$ alkyl) groups, or 1 to 3 $\underline{C_1}$ - $\underline{C_6}$ alkoxy groups; or

 R^7 and R^8 can be taken together to form -(CH₂), L-(CH₂)_r, wherein L is CX^2X^2 , SO,, or NX^2 ; R^9 and R^{10} are each independently selected from the group consisting of hydrogen, fluoro, hydroxy, and C₁-C5 alkyl optionally independently substituted with 1-5 halo groups;

 R^{11} is selected from the group consisting of C_1 - C_5 alkyl and phenyl optionally substituted with 1-3 substituents each independently selected from the group consisting of C_1 - C_5 alkyl, halo, and C_1 - C_5 alkoxy;

 R^{12} is selected from the group consisting of C_1 - C_5 alkylsulfonyl, C_1 - C_5 alkanoyl, and C_1 - C_5 alkylwherein the alkyl portion is optionally independently substituted by 1-5 halo groups;

A¹ for each occurrence is independently selected from the group consisting of C₅-C7 cycloalkenyl, phenyl, a partially saturated, fully saturated, or fully unsaturated 4to 8-membered ring optionally having 1 to 4 heteroatoms independently selected from the group consisting of oxygen, sulfur, and nitrogen, and a bicyclic ring system consisting of a partially saturated, fully unsaturated, or fully USERSNDOCSNLA21952UPAEDWk9901LDQC/212902 - 12 -

saturated 5- or 6 membered ring, optionally having 1 to 4 heteroatoms independently selected from the group consisting of nitrogen, sulfur, and oxygen, fused to a partially saturated, fully saturated, or fully unsaturated 5- or 6-membered ring, optionally having 1 to 4 heteroatoms independently selected from the group consisting of nitrogen, sulfur, and oxygen;

A¹ for each occurrence is independently optionally substituted, on one or optionally both rings if A' is a bicyclic ring system, with up to three substituents, each substituent independently selected from the group consisting of F, Cl, Br, I, OCF₃, OCF₂H, CF₃, CH₃, OCH₃, -OX⁶, -CONX⁶X⁶, - CO₂X⁶, oxo, C₁C₆ alkyl, nitro, cyano, benzyl, -SO_m(C₁-C₆ alkyl), 1 H-tetrazol-5-yl, phenyl, phenoxy, phenylalkyloxy, halophenyl, methylenedioxy, -NX⁶X⁶, - NX⁶COX⁶, -SO₂NX⁶X¹, -NX⁶SO₂-phenyl, NX⁶SO₂X⁶, - CONX¹¹X¹², -SO₂NX¹¹X¹², -NX⁶SO₂X¹², -NX⁶CONX¹¹X¹², -NX⁶SO₂NX¹¹X¹², -NX⁶COX¹², imidazolyl, thiazolyl, and tetrazolyl, provided that if A¹ is optionally substituted with methylenedioxy then it can only be substituted with one methylenedioxy;

wherein X^{11} is hydrogen or C_1 - C_6 alkyl optionally independently substituted with phenyl, phenoxy, C_1 - C_6 alkoxycarbonyl, -SO_M(C_1 - C_6 alkyl), 1 to 5 halo groups, 1 to 3 hydroxy groups, 1 to 3 C_1 - C_1 0 alkoxy groups, or 1 to 3 C_1 - C_6 alkoxy groups;

 X^{12} is hydrogen, C_1 - C_6 alkyl, phenyl, thiazolyl, imidazolyl, fury[, or thienyl, provided that when X^{12} is not hydrogen, the X^{12} group is optionally substituted with one to three substituents independently selected from the group consisting of CI, F, CH₃, OCH₃, OCF₃, and CF₃;

or X" and X'² are taken together to form -(CH2)r-L¹-(CH₂)_r, wherein L¹ is CX²X², O, SO_m or NX²; r for each occurrence is independently 1, 2, or 3;

 X^2 for each occurrence is independently hydrogen, optionally substituted C_1 - C_6 alkyl, or optionally substituted C_3 - C_7 cycloalkyl, wherein the optionally substituted C_1 - C_6 alkyl and optionally substituted C_3 - C_1 cycloalkyl in the definition of X^2 are optionally independently substituted with - $SO_m(C_1$ - C_6 alkyl), - $CO2 X^3$, 1 to 5 halo groups, or 1-3 OX^3 groups;

X³ for each occurrence is independently hydrogen or C₁-C₆ alkyl;

 X^6 for each occurrence is independently hydrogen, optionally substituted C_1 - C_6 alkyl, halogenated C_2 - C_6 alkyl, optionally substituted C_3 - C_7 cycloalkyl, halogenated C_3 - C_7 cycloalkyl, wherein the optionally substituted C_1 - C_6 alkyl and optionally substituted C_3 - C_7 cycloalkyl in the definition of X^6 are optionally independently mono-or di-substituted with C_1 - C_4 alkyl, hydroxy, C_1 - C_4 alkoxy, carboxyl, CONH₂, -

SO_m(C₁C₆ alkyl), carboxylate (C₁-C₄ alkyl) ester, or 1 H-tetrazol-5-yl; or

when there are two X^6 groups on one atom and both X^6 are independently C_1C_6 alkyl, the two C_1-C_6 alkyl groups may be optionally joined, and together with the atom to which the two X^6 groups are attached, form a 4- to 9- membered ring optionally having oxygen, sulfur, or NX^7 as a ring member, wherein X^7 is hydrogen or C_1-C_6 alkyl optionally substituted with hydroxy;

m for each occurrence is independently O, 1, or 2; with the provisos that:

X⁶ and X'2 cannot be hydrogen when attached to CO or SO₂ in the form COX⁶, COX'², SO2 X⁶ or SO₂X'²; and

when R⁶ is a bond then L is NX² and each r in the definition -(CH₂), L-(CH₂), is independently 2 or 3.

5. (Withdrawn) A pharmaceutical composition according to claim 1 wherein said corticotropin releasing factor antagonist is a compound of formula

and the pharmaceutically acceptable acid addition salts thereof, wherein A is N or - CR_6 ;

B is $-NR_1R_2$, $-CR_1R_2R_{11}$, $-C(=CR_2R_{12})R_1$, $-NHCHR_1R_2$, $-OCHR_1R_2$, $-SCHR_1R_2$, $-CHR_2OR_{12}$, $-CHR_2SR_{12}$, $-C(S)R_1$ or $-C(O)R_1$;

 R_1 is C_1 - C_6 alkyl which may optionally be substituted with one or two substituents independently selected from the group consisting of hydroxy, fluoro, chloro, bromo, iodo, C_1 - C_4 alkoxy, -O-CO- $(C_1$ - C_4 alkyl), -O-CO-NH(C_1 - C_4 alkyl), -O-CO-N(C_1 - C_4 alkyl)(C_1 - C_2 alkyl), -NH(C_1 - C_4 alkyl), -N(C_1 - C_4 alkyl)(C_1 - C_4 alkyl), -NHCO(C_1 - C_4 alkyl), -COO(C_1 - C_4 alkyl), -CON(C_1 - C_4 alkyl), CON(C_1 - C_4 alkyl), CN, NO₂, -SO(C_1 - C_4 alkyl), -SO₂(C_1 - C_4 alkyl), and wherein any of the foregoing C_1 - C_4 alkyl and C_1 - C_6 alkyl groups may optionally contain one carbon-carbon double or triple bond;

R₂ is C₁-C₁₂ alkyl, aryl, -(C₁-C₄ alkylene)aryl wherein said aryl is phenyl, naphthyl, thienyl, benzothienyl, pyridyl, quinolyl, pyrazinyl, pyrimidyl, imidazolyl, furanyl, benzofuranyl, benzothiazolyl, isothiazolyl, benzisothiazolyl, thiazolyl, isoxazolyl, benzisoxazolyl, benzimidazolyl, triazolyl, pyrazolyl, pyrrolyl, indolyl, oxazolyl, or benzoxazolyl; or 3- to 8- membered cycloalkyl or -(C₁-C₆ alkylene)cycloalkyl, wherein one or two of the ring carbons of said cycloalkyl having at least 4 ring members and the cycloalkyl moiety of said -(C₁-C₆ alkylene)cycloalkyl having at least 4 ring members may optionally be replaced by an oxygen or sulfur atom or by N-Z wherein Z is hydrogen; or C₁-C₄ alkyl, and wherein each of said groups R2 may optionally be substituted with from one to three substituents independently selected from chloro, fluoro, and C₁-C₄ alkyl, or by one substituent selected from bromo, iodo, C₁-C₆ alkoxy, -O-CO-(C₁-C₆ alkyl), ⁻S(C₁-C₆ alkyl), -COO(C₁-C₄ alkyl), CN. NO_2 , $-SO(C_1-C_4$ alkyl), and $-SO_2(C_1-C_4$ alkyl), and wherein said C_1-C_{12} alkyl and the C_1-C_4 alkylene moiety of said -(C₁-C₄ alkylene)aryl may optionally contain one carbon-carbon double or triple bond; or -NR₁R₂ may form a saturated 5- to 8-membered heterocyclic ring, or -CHR₁R₂ may form a saturated 5- to 8-membered carbocyclic ring, wherein each of these rings may optionally contain one or two carbon-carbon double bonds and wherein one or two of the carbon atoms of each of these rings may optionally be replaced with a sulfur or oxygen atom;

 R_3 is C_1 - C_4 alkyl, fluoro, chloro, bromo, iodo, - CH_2OH , - CH_2OCH_3 , - $O(C_1$ - C_3 alkyl), - $S(C_1$ - C_3 alkyl), or - $SO_2(C_1$ - C_3 alkyl), wherein said C1- C_3 alkyl may optionally contain one carbon-carbon double or triple bond;

R₄ is hydrogen, C₁-C₆ alkyl, fluoro, chloro, bromo, iodo, C₁-C₄ alkoxy, amino, -NHCH₃, -N(CH₃)₂, - USERS\DOCS\La2

CH₂OH, -CH₂OCH₃, or -SO_n(C₁-C₄ alkyl), wherein n is O, 1 or 2, cyano, hydroxy, -CO(C₁-C₄ alkyl), -CHO, Or -COO(C₁-C₄ alkyl) wherein the C₁-C₄ alkyl moieties in the foregoing R₄ groups may optionally contain one carbon-carbon double or triple bond;

 R_5 is phenyl, naphthyl, thienyl, benzothienyl, pyridyl, pyrimidyl, benzofuranyl, pyrazinyl or benzothiazolyl, wherein each one of said groups R_5 may optionally be substituted with from one to three substituents independently selected from fluoro, chloro, C_1 - C_6 alkyl and C_1 - C_6 alkoxy, or by one substituent selected from iodo, hydroxy, bromo, formyl, cyano, nitro, amino, trifluoromethyl, -NH(C_1 - C_4 alkyl), -N(C_1 - C_6)(C_1 - C_2 alkyl), -COO(C_1 - C_4 alkyl), -CO(C_1 - C_4 alkyl), -COON, -SO₂NH(C_1 - C_4 alkyl), -SO₂N(C_1 - C_6 alkyl), -SO₂NH₂, -NHSO₂(C_1 - C_4 alkyl), -S(C_1 - C_6 alkyl) and -SO₂(C_1 - C_6 alkyl), wherein each of said C_1 - C_4 alkyl and C_1 - C_6 alkyl moieties in the foregoing R^5 groups may optionally be substituted with one to three fluorine atoms:

 R_6 is hydrogen, C_1 - C_4 alkyl, fluoro, chloro, bromo, iodo, - CH_2OH , - CH_2OCH_3 , or C_1 - C_4 alkoxy; R_7 is hydrogen, C_1 - C_4 alkyl, fluoro, chloro, bromo, iodo, - $O(C_1$ - C_4 alkyl), cyano, - CH_2OH , - $CH_2O(C_1$ - C_2 alkyl), - $CO(C_1$ - C_2 alkyl), or - $CO(C_1$ - C_2 alkyl);

R₁₁is hydrogen, hydroxy, fluoro, or methoxy; and

R₁₂ is hydrogen or C₁-C₄ alkyl;

with the proviso that when A is N, then: (a) B is not unsubstituted alkyl; (b) R_5 is not unsubstituted phenyl or monosubstituted phenyl; and (c) R_3 is not unsubstituted alkyl; or a pharmaceutically acceptable salt of such compound.

6. (Withdrawn) A pharmaceutical composition according to claim 1 wherein said corticotropin releasing factor antagonist is a compound of formula

$$R^3$$
 A
 D
 $E^{--}G$
 R^3
 A
 D
 $E^{--}G$
 ZR^5

or

$$R^3$$
 A
 D
 E^-G
 ZR^5

or a pharmaceutically acceptable salt thereof, wherein

the dashed lines represent optional double bonds;

A is nitrogen or CR⁷;

B is $-NR^1R^2$, $-CR^1R^2R^{10}$, $-C(=CR^2R^{11})R^1$, $-NHCR^1R^2R^{10}$, $-OCR^1R^2R^{10}$, $-SCR^1R^2R^{10}$, $-CR^2R^{10}NHR^1$, $-CR^2R^{10}OR^1$, $-CR^2R^{10}SR^1$ or $-COR^2$;

D is nitrogen and is single bonded to all atoms to which it is attached, or D is carbon and is either double bonded to E in formulas I and II or double bonded to the adjacent carbon atom common to both fused rings in formula III, or D is CH and is single bonded to E in formulas I and II;

E is nitrogen, CH or carbon;

F is oxygen, sulfur, CHR⁴ or NR ⁴ when it is single bonded to E and F is nitrogen or CR⁴ when it is double bonded to E:

G, when single bonded to E, is hydrogen, C_1 - C_4 alkyl, -S(C_1 - C_4 alkyl), -O(C_1 - C_4 alkyl), NH₂, -NH(C_1 - C_4 alkyl) or -N(C_1 - C_2 alkyl)(C_1 - C_4 alkyl), wherein each of the C_1 - C_4 alkyl groups of G may optionally be substituted with one hydroxy, -O(C_1 - C_2 alkyl) or fluoro group; G, when double bonded to E, is oxygen, sulfur or NH; and G, when E is nitrogen and double bonded to D or F, is absent;

the C₁-C₄ alkyl groups in the foregoing R' groups may optionally contain one or two double or triple bonds;

R2 is C1-C12 alkyl which may optionally contain from one to three double or triple bonds, aryl or (C1-C4 alkylene)aryl, wherein said aryl and the aryl moiety of said (C₁-C₄ alkylene)aryl is selected from phenyl, naphthyl, thienyl, benzothienyl, pyridyl, quinolyl, pyrazinyl, pyrimidinyl, imidazolyl, furanyl, benzofuranyl, benzothiazolyl, isothiazolyl, pyrazolyl, pyrrolyl, indolyl, pyrrolopyridyl, oxazolyl and benzoxazolyl; C₃-C₈ cycloalkyl or (C₁-C₆ alkylene)(C₃-C₈ cycloalkyl), wherein one or two of the carbon atoms of said cycloalkyl and the 5 to 8 membered cycloalkyl moieties of said (C₁-C₆ alkylene)(C3-CS cycloalkyl) may optionally and independently be replaced by an oxygen or sulfur atom or by NZ² wherein Z² is selected from hydrogen, C₁-C₄ alkyl, benzyl and C₁-C₄ alkanoyl, and wherein each of the foregoing R² groups may optionally be substituted with from one to three substituents independently selected from chloro, fluoro, hydroxy and C₁-C₄ alkyl, or with one substituent selected from bromo, iodo, C_1 - C_6 alkoxy, -OC(=O)(C_1 - C_6 alkyl), -OC(=O)N(C_1 - C_4 alkyl)(C_1 - C_2 alkyl), -S(C_1 - C_6 alkyl), amino, - $NH(C_1-C_2 \text{ alkyl}), -N(C_1-C_2 \text{ alkyl})(C_1-C_4 \text{ alkyl}), -N(C_1-C_4 \text{ alkyl})-CO-(C_1-C_4 \text{ alkyl}), -NHCO(C_1-C_4 \text{ alkyl}), -NHCO(C_1$ COON, $-COO(C_1-C_4 \text{ alkyl})$, $-CONH(C_1-C_4 \text{ alkyl})$, $-CON(C_1-C_4 \text{ alkyl})(C_1-C_2 \text{ alkyl})$, -SH, -CN, $-NO_2$, - $SO(C_1-C_4 \text{ alkyl})$, $-SO_2(C_1-C_4 \text{ alkyl})$, $-SO_2NH(C_1-C_4 \text{ alkyl})$ and $-SO_2N(C_1-C_4 \text{ alkyl})$ ($C_1-C_2 \text{ alkyl}$); -NR'R² or CR'R²R' may form a saturated 3 to 8 membered carbocyclic ring which may optionally contain from one to three double bonds and wherein one or two of the ring carbon atoms of such 5 to 8 membered rings may optionally and independently be replaced by an oxygen or sulfur atom or by NZ³ wherein Z³ is hydrogen, C₁-C₄ alkyl, benzyl or C₁-C₄ alkanoyl; R3 is hydrogen, C1-C4 alkyl, -O(C1-C4 alkyl), chloro, fluoro, bromo, iodo, -CN, -S(C1-C4 alkyl) or -SO₂(C₁-C₄ alkyl) wherein each of the (C₁-C₄ alkyl) moieties in the foregoing R³ groups may optionally be substituted with one substituent R9 selected from hydroxy, fluoro and (C1-C2 alkoxy);

each R^4 is, independently, hydrogen, $(C_1\text{-}C_6\,\text{alkyl})$, fluoro, chloro, bromo, iodo, hydroxy, cyano, amino, nitro, $-O(C_1\text{-}C_4\,\text{alkyl})$, $-N(C_1\text{-}C_4\,\text{alkyl})$, $-C_2\,\text{alkyl}$, $-S(C_1\text{-}C_4\,\text{alkyl})$, $-S(C_1\text{-}C_4\,\text{alkyl})$, $-S(C_1\text{-}C_4\,\text{alkyl})$, $-S(C_1\text{-}C_4\,\text{alkyl})$, wherein each of the $(C_1\text{-}C_6\,\text{alkyl})$ and $(C_1\text{-}C_4\,\text{alkyl})$ moieties in the foregoing R^4 groups may optionally contain one or two double or triple bonds and may optionally be substituted with one or two substituents independently selected from hydroxy, amino, $C_1\text{-}C_3\,\text{alkoxy}$, dimethylamino, methylamino, ethylamino, -NHC(=O)CH₃, fluoro, chloro, $C_1\text{-}C_3\,\text{thioalkyl}$, -CN, -COON, -C(=O)O($C_1\text{-}C_4\,\text{alkyl}$), -C(=O)($C_1\text{-}C_4\,\text{alkyl}$) and -NO₂;

 R^5 is phenyl, naphthyl, thienyl, benzothienyl, pyridyl, quinolyl, pyrazinyl, furanyl, benzofuranyl, benzothiazolyl, benzisothiazolyl, benzisoxazolyl, benzimidazolyl, indolyl, benzoxazolyl or C_3 - C_8 cycloalkyl wherein one or two of the carbon atoms of said cycloalkyl rings that contain at least 5 ring members may optionally and independently be replaced by an oxygen or sulfur atom or by NZ^4 wherein Z^4 is hydrogen, C_1 - C_4 alkyl or benzyl; and wherein each of the foregoing R^5 groups is substituted with from one to four substituents R^{12} wherein one to three of said substituents

may be selected, independently, from chloro, C_1 - C_6 alkyl and -O(C_1 - C_6 alkyl) and one of said substituents may be selected from bromo, iodo, formyl, -CN, -CF₃, -NO₂, -NH₂, -NH(C_1 - C_4 alkyl), -N(C_1 - C_2 alkyl)(C_1 - C_6 alkyl), -C(=O)O(C_1 - C_4 alkyl), -C(=O)(C_1 - C_4 alkyl), -COON, -SO₂NH(C_1 - C_4 alkyl), -SO₂N(C_1 - C_2 alkyl)(C_1 - C_4 alkyl), -SO₂NH₂, -NHSO₂(C_1 - C_4 alkyl), -S(C_1 - C_6 alkyl) and -SO₂(C_1 - C_6 alkyl), and wherein each of the C_1 - C_4 alkyl and C_1 - C_6 alkyl moieties in the foregoing R⁵ groups may optionally be substituted with one or two substituents independently selected from fluoro, hydroxy, amino, methylamino, dimethylamino and acetyl;

 R^7 is hydrogen, C_1 - C_4 alkyl, halo, cyano, hydroxy, -O(C_1 - C_4 alkyl) -C(=O)(C_1 - C_4 alkyl), -C(=O)O(C_1 - C_4 alkyl), -OCF₃, -CF₃, -CH₂OH, -CH₂O(C_1 - C_4 alkyl);

R¹⁰ is hydrogen, hydroxy, methoxy or fluoro;

R¹¹is hydrogen or C₁-C₄ alkyl; and

Z is NH, oxygen, sulfur, $-N(C_1-C_4 \text{ alkyl})$, $-NC(=O)(C_1-C_2 \text{ alkyl})$, $NC(=O)O(C_1-C_2 \text{ alkyl})$ or $CR^{13}R^{14}$ wherein R^{13} and R^{14} are independently selected from hydrogen, trifluoromethyl and methyl with the exception that one of R^{13} and R^{14} can be cyano;

with the proviso that: (a) in the five membered rings of structures I, II and III, there can not be two double bonds adjacent to each other; and (b) when R⁴ is attached to nitrogen, it is not halo, cyano or nitro;

or a pharmaceutically acceptable salt of such compound.

7. (Withdrawn) A pharmaceutical composition according to claim 1 wherein said corticotropin releasing factor antagonist is a compound of formula

wherein the dashed lines represent optional double bonds:

A is nitrogen or CR7:

B is $-NR^1R^2$, $-CR^1R^2R^{10}$, $-C(=CR^2R^{11})R^1$, $-NHCR^1R^2R^{11}$, $-OCR^1R^2R^{10}$, $-SCR^1R^2R^{10}$, $-CR^2R^{10}NHR^1$, $-CR^2R^{10}OR^1$, $-CR^2R^{10}SR^1$ or $-COR^2$, and is single bonded to D; or B is $-CR^1R^2$, and is double bonded to D and D is carbon;

D is nitrogen or CR⁴ and is single bonded to all atoms to which it is attached, or D is carbon and is double bonded to E or double bonded to B;

E is oxygen, nitrogen, sulfur, C=O, C=S, CR⁶R¹², NR⁶ or CR⁶; or E is a two atom spacer, wherein one of the atoms is oxygen, nitrogen, sulfur, C=O, C=S, CR⁶R¹², NR⁶ or CR⁶, and the other is CR⁶R¹² or CR⁹;

K and G are each, independently, C=O, C=S, sulfur, oxygen, CHR⁸ or NR⁸ when single bonded to both adjacent ring atoms, or nitrogen or CR⁸ when it is double bonded to an adjacent ring atom;

the 6- or 7-membered ring that contains D, E, K and G may contain from one to three double bonds, from zero to two heteroatoms selected from oxygen, nitrogen and sulfur, and from zero to two C=O or C=S groups, wherein the carbon atoms of such groups are part of the ring and the oxygen and sulfur atoms are substituents on the ring;

 R^1 is C_1 - C_6 alkyl optionally substituted with from one or two substituents independently selected from hydroxy, fluoro, chloro, bromo, iodo, C_1 - C_4 alkoxy, CF_3 , $-C(=O)(C_1$ - C_4 alkyl), -C(=O)-O- $(C_1$ - C_4) alkyl, $-OC(=O)(C_1$ - C_4 alkyl), $-OC(=O)N(C_1$ - C_4 alkyl)(C_1 - C_2 alkyl), $-NHCO(C_1$ - C_4 alkyl), -COON, $-COO(C_1$ - C_4 alkyl), $-CONH(C_1$ - C_4 alkyl), $-CON(C_1$ - C_4 alkyl)(C_1 - C_2 alkyl), $-S(C_1$ - C_4 alkyl), $-SO_2(C_1$ - C_4 alkyl), $-SO_2(C_1$ - C_4 alkyl), $-SO_2NH(C_1$ - C_4 alkyl) and $-SO_2N(C_1$ - C_4 alkyl)(C_1 - C_2 alkyl), wherein each of the C_1 - C_4 alkyl groups in the foregoing R^1 groups may optionally contain one or two double or triple bonds;

R² is C₁-C₁₂ alkyl which may optionally contain from one to three double or triple bonds, aryl or (C₁-C₄ alkylene)aryl, wherein said aryl and the aryl moiety of said (C₁-C₄ alkylene)aryl is selected from phenyl, naphthyl, thienyl, benzothienyl, pyridyl, quinolyl, pyrazinyl, pyrimidinyl, imidazolyl, furanyl, benzofuranyl, benzothiazolyl, isothiazolyl, pyrazolyl, pyrrolyl, indolyl, pyrrolopyridyl, oxazolyl and benzoxazolyl; C₃-C₈ cycloalkyl or (C₁-C₆ alkylene)(C₃-C₈ cycloalkyl), wherein one or two of the carbon atoms of said cycloalkyl and the 5 to 8 membered cycloalkyl moieties of said (C₁-C₆ alkylene)(C₃-C₈ cycloalkyl may optionally and independently be replaced by an oxygen or sulfur and wherein each of the foregoing R² groups may optionally be substituted with from one to three substituents independently selected from chloro, fluoro, hydroxy and C₁-C₄ alkyl, or with one substituent selected from C_1 - C_6 alkoxy, $-OC(=O)(C_1$ - C_6 alkyl), $-OC(=O)N(C_1$ - C_4 alkyl)(C_1 - C_2 alkyl), $-S(C_1$ - C_6 alkyl), amino, -NH(C_1 -CZ alkyl), -N(C_1 -CZ alkyl)(C_1 -C4 alkyl), -N(C_1 -C4 alkyl)-CO-(C_1 -C4 alkyl), -NHCO(C_1 -C4 alkyl), -COON, -COO(C1-C4 alkyl), -CONH(C1-C4 alkyl), -CON(C1-C4 alkyl)(C1-C2 alkyl), -SH, -CN, -NO2, - $SO(C_1-C_4 \text{ alkyl})$, $-SO_2(C_1-C_4 \text{ alkyl})$, $-SO_2NH(C_1-C_4 \text{ alkyl})$ and $-SO_2N(C_1-C_4 \text{ alkyl})(C_1-C_2 \text{ alkyl})$; -NR'R² or CR'R²R' may form a ring selected from saturated 3 to 8 membered rings, the 5 to 8 membered rings of which may optionally contain one or two double bonds, and wherein one or two of the ring carbon atoms of such 5 to 8 membered rings may optionally and independently be replaced by an oxygen or sulfur atom or by NZ³ wherein Z³ is hydrogen or C₁-C₄ alkyl; R³ is hydrogen, C₁-C₄ alkyl, -O(C₁-C₄ alkyl), chloro, fluoro, bromo, iodo, -S(C₁-C₄ alkyl) or -SO₂(C₁-C₄

R⁴ is hydrogen, C₁-C₂ alkyl, hydroxy or fluoro;

each R^6 , R^8 and R^9 that is attached to a carbon atom is selected, independently, from hydrogen, C_1 - C_2 alkyl, fluoro, chloro, bromo, iodo, hydroxy, hydroxymethyl, formyl, trifluoromethyl, cyano, amino, nitro, - $O(C_1$ - C_2 alkyl), - $N(C_1$ - C_2 alkyl), - $S(C_1$ - C_2 alkyl), wherein each of the C_1 - C_2 alkyl moieties in the foregoing R^6 , R^8 , and R^9 groups may optionally contain one double or triple bond; and each R^6 , R^8 , and R^9 that is attached to a nitrogen atom is selected, independently, from hydrogen and C_1 - C_4 alkyl;

R⁵ is substituted phenyl, naphthyl, pyridyl or pyrimidyl, wherein each of the foregoing R⁵ groups is

alkyl);

substituted with from two to four substituents R^{S} , wherein from one to three of said substituents may be selected, independently, from chloro, C_1 - C_6 alkyl, $-O(C_1$ - C_6 alkyl) and $-(C_1$ - C_6 alkylene) $O(C_1$ - C_6 alkyl), and wherein one of said substituents may be selected, independently, from bromo, iodo, formyl, cyano, trifluoromethyl, nitro, amino, $-NH(Cl-C_4$ alkyl), $-N(C_1-C_2$ alkyl)(C_1 - C_6 alkyl), $-C(=O)O(C_1-C_4$ alkyl), $-C(=O)(C_1-C_4$ alkyl), $-C(=O)(C_1-C_4$ alkyl), $-SO_2NH(C_1-C_4$ alkyl), $-SO_2NH(C_1-C_4$ alkyl), and wherein each of the C_1 - C_4 alkyl and C_1 - C_6 alkyl moieties in the foregoing R^5 groups may optionally be substituted with one or two substituents independently selected from fluoro, hydroxy, amino, methylamino, dimethylamino and acetyl;

 R^7 is hydrogen, methyl, halo, hydroxy, methoxy, -C(=O)(C₁-C2 alkyl), -C(=O)O(C₁-C2 alkyl), trifluoromethoxy, hydroxymethyl, trifluoromethyl or formyl;

R¹⁰ is hydrogen, hydroxy, methoxy or fluoro;

R¹¹ is hydrogen or C₁-C₄ alkyl;

R¹² is hydrogen or methyl; and

Z is NH, oxygen, sulfur, -N(C_1 - C_4 alkyl), or $CR^{13}R^{14}$ wherein R^{13} and R^{14} are independently selected from hydrogen, and methyl with the exception that one of R^{13} and R^{14} may optionally be cyano; with the proviso that: (a) in the six or seven membered rings of structures in formula I, there can not be two double bonds adjacent to each other; and (b) when D is carbon and is double bonded to B, then B is CR^1R^2 :

or a pharmaceutically acceptable salt of such compound.

8. (Withdrawn) A pharmaceutical composition according to claim 1 wherein said corticotropin releasing factor antagonist is a compound of

$$R^3$$
 N
 K
 G
 R_5

or a pharmaceutically acceptable salt thereof,

wherein the dashed lines represent optional double bonds;

A is nitrogen or CR⁷:

B is $-NR^1R^2$, $-CR^1R^2R^{10}$ $-C(=CR^2R^{11})R^1$, $-NHCR^1R^2R^{10}$, $-OCR^1R^2R^{10}$, $-SCR^1R^2R^{10}$, $-CR^2R^{10}NHR^1$, $-CR^2R^{10}OR^1$, $-CR^2R^{10}SR^1$ or $-COR^2$:

J and K are each independently nitrogen or carbon and both J and K are not 15 nitrogens;

D and E are each selected, independently, from nitrogen, CR⁴, C=O, C=S, sulfur, oxygen, CR⁴ R⁶ and NR⁸;

G is nitrogen or carbon;

the ring containing D, E, G, K, and J in formula I may be a saturated or unsaturated 5-membered ring

and may optionally contain one or two double bonds and may optionally contain from one to three heteroatoms in the ring and may optionally have one or two C=O or C=S groups: R¹ is C₁-C₆ alkyl optionally substituted with one or two substituents independently selected from hydroxy, fluoro, chloro, bromo, iodo, -O-(C₁-C₄ alkyl), CF₃, -C(=O)O-(C₁-C₄alkyl), -OC(=O)(C₁-C4 alkyl), -OC(=O)N(C1-C4 alkyl)(C1-C2 alkyl), -NHCO(C1-C4 alkyl), -COON, -COO(C1-C4 alkyl), - $CONH(C_1-C_4 \text{ alkyl}), -CON(C_1-C_4 \text{ alkyl})(C_1-C_2 \text{ alkyl}), -S(C_1-C_4 \text{ alkyl}), -CN, -NO_2, -SO(C_1-C_4 \text{ alkyl}), -CN_2 \text{$ $SO_2(C_1-C_4 \text{ alkyl})$, $-SO_2NH(C_1-C_4 \text{ alkyl})$ and $-SO_2N(C_1-C_4 \text{ alkyl})(C_1-C_2 \text{ alkyl})$, wherein each of the C_1-C_4 alkyl groups in the foregoing R' groups may optionally contain one or two double or triple bonds; R² is C₁-C12 alkyl which may optionally contain from one to three double or triple bonds, aryl or (C₁-C₄ alkylene)aryl, wherein said aryl and the aryl moiety of said (C₁-C₄ alkylene)aryl is selected from phenyl, naphthyl, thienyl, benzothienyl, pyridyl, quinolyl, pyrazinyl, pyrimidinyl, imidazolyl, furanyl, benzofuranyl, benzothiazolyl,isothiazolyl, pyrazolyl, pyrrolyl, indolyl, pyrrolopyridyl, oxazolyl and benzoxazolyl; C₃-C₈ cycloalkyl or (C₁-C₆ alkylene)(C₃-C₈ cycloalkyl), wherein one or two of the carbon atoms of said cycloalkyl and the 5 to 8 membered cycloalkyl moieties of said (C₁-C₆ alkylene)(C₃-C_a cycloalkyl) may optionally and independently be replaced by an oxygen or sulfur atom or by NZ2 wherein Z² is selected from hydrogen, C₁-C₄ alkyl, benzyl and C₁-C₄ alkanoyl, and wherein each of the foregoing R² groups may optionally be substituted with from one to three substituents independently selected from chloro, fluoro, hydroxy and C₁-C₄ alkyl, or with one substituent selected from bromo. iodo, C_1 - C_6 alkoxy, -OC(=O)(C_1 -C6 alkyl), -OC(=O)N(C_1 -C4 alkyl)(C_1 - C_2 alkyl), -S(C_1 - C_6 alkyl), amino, $-NH(C_1-C_2 \text{ alkyl}), -N(C_1-C_2 \text{ alkyl})(C_1-C_4 \text{ alkyl}), -N(C_1-C_4 \text{ alkyl})-CO-(C_1-C_4 \text{ alkyl}), -NHCO(C_1-C_4 \text{ alkyl}), -NHCO(C_$ COON, -OOO(C_1 - C_4 alkyl), -CONH(C_1 - C_4 alkyl), -CON(C_1 - C_4 alkyl)(C_1 - C_2 alkyl), -SH, -CN, -NO₂, - $SO(C_1-C_4 \text{ alkyl})$, $-SO_2(C_1-C_4 \text{ alkyl})$, $-SO_2NH(C_1-C_4 \text{ alkyl})$ and $-SO_2N(C_1-C_4 \text{ alkyl})$ ($C_1-C_2 \text{ alkyl}$); -NR¹R² or CR¹R²R¹⁰ may form a saturated 3 to 8 membered carbocyclic ring which may optionally contain from one to three double bonds and wherein one or two of the ring carbon atoms of such 5 to 8 membered rings may optionally and independently be replaced by an oxygen or sulfur atom or by

 R^3 is hydrogen, C_1 - C_4 alkyl, -O(C_1 - C_4 alkyl), chloro, fluoro, bromo, iodo, (C_1 - C_2 alkylene)-O-(C_1 - C_2 alkyl), (C_1 - C_2 alkylene)-OH, or -S(C_1 - C_4 alkyl);

NZ³ wherein Z³ is hydrogen, C₁-C₄ alkyl, benzyl or C₁-C₄ alkanoyl;

each R^4 is, independently, hydrogen, (C_1 - C_6 alkyl), fluoro, chloro, bromo, iodo, hydroxy, cyano, amino, (C_1 - C_2 alkylene)-OH, CF₃, CH₂SCH₃, nitro, -O(C_1 - C_4 alkyl), -N(C_1 - C_4 alkyl), -C(=O)H or -C(=O)O(C_1 - C_4 alkyl);

R⁶ is hydrogen, methyl or ethyl;

R⁸ is hydrogen or C₁-C₄ alkyl;

 R^5 is phenyl, pyridyl, pyrazinyl, pyrimidyl, pyridazinyl and wherein each of the foregoing R^5 groups is substituted with from one to four substituents R^{13} wherein one to three of said substituents may be selected, independently, from fluoro, chloro, C_1 - C_6 alkyl and -O(C_1 - C_6 alkyl) and one of said substituents may be selected from bromo, iodo, formyl, OH, (C_1 - C_4 alkylene)-OH, (C_1 - C_4 alkyl), -CN, -CF₃, -NO₂, -NH₂, -NH(C_1 - C_4 alkyl), -N(C_1 - C_2 alkyl), -OCO(C_1 - C_4 alkyl), -OCO(C_1 - C_4 alkyl),

 $(C_1-C_4 \text{ alkylene}) - O - (C_1-C_4 \text{ alkyl}), -S(C_1-C_6 \text{ alkyl}), (C_1-C_4 \text{ alkylene}) - S - (C_1-C_4 \text{ alkyl}), -C(=O)O(C_1-C_4 \text{ alkyl}), -C(=O)O(C_1-C_4 \text{ alkyl}), -SO_2NH(C_1-C_4 \text{ alkyl}), -SO_2NH(C_1-C_2 \text{ alkyl})(C_1-C_4 \text{ alkyl}), -SO_2NH_2, -NHSO_2(C_1-C_4 \text{ alkyl}), -S(C_1-C_6 \text{ alkyl}) \text{ and } -SO_2(C_1-C_6 \text{ alkyl}), \text{ and wherein each of the } C_1-C_4 \text{ alkyl} \text{ and } C_1-C_6 \text{ alkyl} \text{ moieties in the foregoing } R^5 \text{ groups may optionally have one or two double bonds; } R^7 \text{ is hydrogen, } C_1-C_4 \text{ alkyl}, \text{ halo (e.g., chloro, fluoro, iodo or bromo), hydroxy, -O(C_1-C_4 \text{ alkyl}), -C(=O)O(C_1-C_4 \text{ alkyl}), -OCF_3, -CF_3, -CH_2OH \text{ or } -CH_2O(C_1-C_2 \text{ alkyl}); } R^{10} \text{ is hydrogen, hydroxy, methoxy or fluoro; }$

R¹¹is hydrogen or C₁-C₄ alkyl; and

with the proviso that: a) when both J and K are carbons and D is CR⁴ and E is nitrogen, then G can not be nitrogen; (b) when both J and K are carbons and D and G are nitrogens, then E can not be CR⁴ or C=O or C=S; (c) when both J and K are carbons and D and E are carbons, then G can not be nitrogen; (d) when G is carbon, it must be double banded to E; and (e) in the ring containing J, K, D, E and G, there can not be two double bonds adjacent to each other;

and the pharmaceutically acceptable salts of such compounds or a pharmaceutically acceptable salt of such compound.

9. (Withdrawn) A pharmaceutical composition according to claim 1 wherein said corticotropin releasing factor antagonist is a compound of formula

wherein the dashed lines represent optional double bonds;

A is nitrogen or CR7:

B is $-NR^1R^2$, $-CR^1R^2R^{10}$, $-C(=CR^2R^{11})R^1$, $-NHCR^1R^2R^{10}$, $-OCR^1R^2R^{10}$, $-SCR^1R^2R^{10}$, $-CR^2R^{10}NHR^1$, $-CR^2R^{10}OR^1$, $-CR^2R^{10}SR^1$ or $-COR^2$:

G is nitrogen or CR⁴ and is single bonded to all atoms to which it is attached, or G is carbon and is double bonded to K;

K is nitrogen or CR⁶ when double bonded to G or E, or K is oxygen, sulfur, C=O, C=S, CR⁶R¹² or NR⁸ when single bonded to both adjacent ring atoms, or K is a two atom spacer, wherein one of the two ring atoms of the spacer is oxygen, nitrogen, sulfur, C=O, C=S, CR⁶R¹², NR⁶ or CR⁶, and the other is CR⁶R¹² or CR⁹:

D and E are each, independently, C=O, C=S, sulfur, oxygen, CR⁴R⁶ or NR⁸ when single bonded to both adjacent ring atoms, or nitrogen or CR⁴ when it is double bonded to an adjacent ring atom;

the 6- or 7-membered ring that contains D, E, K and G may contain from one to three double bonds, from zero to two heteroatoms selected from oxygen, nitrogen and sulfur, and from zero to

two C=O or C=S groups, wherein the carbon atoms of such groups are part of the ring and the oxygen and sulfur atoms are substituents on the ring;

 R^1 is C_1 - C_6 alkyl optionally substituted with from one or two substituents independently selected from hydroxy, fluoro, chloro, bromo, iodo, Cl^*C_4 alkoxy, CF_3 , $-C(=O)(C_1$ - C_4 alkyl), -C(=O)- $O-(C_1$ - C_4) alkyl, $-OC(=O)(C_1$ - C_4 alkyl), $-OC(=O)N(C_1$ - C_4 alkyl)(C_1 - C_2 alkyl), $-NHCO(C_1$ - C_4 alkyl), -CON, $-COO(C_1$ - C_4 alkyl), $-CONH(C_1$ - C_4 alkyl), $-CON(C_1$ - C_4 alkyl)(C_1 - C_4 alkyl), $-S(C_1$ - C_4 alkyl), $-SO_2(C_1$ - C_4 alkyl), $-SO_2(C_1$ - C_4 alkyl), and $-SO_2N(C_1$ - C_4 alkyl)(C_1 - C_2 alkyl), wherein each of the C_1 - C_4 alkyl groups in the foregoing R' groups may optionally contain one or two double or triple bonds;

 R^2 is C_1 - C_{12} alkyl which may optionally contain from one to three double or triple bonds, aryl or $(C_1$ - C_4 alkylene)aryl, wherein said aryl and the aryl moiety of said $(C_1$ - C_4 alkylene)aryl is selected from phenyl, naphthyl, thienyl, benzothienyl, pyridyl, quinolyl, pyrazoyl, pyrimidinyl, imidazolyl, furanyl, benzofuranyl, benzothiazolyl, isothiazolyl, pyrazolyl, pyrrolyl, indolyl, pyrrolopyridyl, oxazolyl and benzoxazolyl; C_3 - C_8 cycloalkyl or $(C_1$ - C_6 alkylene) $(C_3$ - C_8 cycloalkyl, wherein one or two of the carbon atoms of said cycloalkyl and the 5 to 8 membered cycloalkyl moieties of said $(C_1$ - C_6 alkylene) $(C_3$ - C_8 cycloalkyl may optionally and independently be replaced by an oxygen or sulfur atom or by NZ wherein Z is hydrogen, C_1 - C_4 alkyl or benzyl, and wherein each of the foregoing R^2 groups may optionally be substituted with from one to three substituents independently selected from chloro, fluoro, hydroxy and C_1 - C_4 alkyl, or with one substituent selected from C_1 - C_6 alkoxy, $-OC(=O)(C_1$ - C_6 alkyl), $-OC(=O)N(C_1$ - C_4 alkyl) $(C_1$ - C_2 alkyl), $-S(C_1$ - C_6 alkyl), amino, $-NH(C_1$ - C_2 alkyl), $-N(C_1$ - C_2 alkyl), $-CON(C_1$ - C_4 alkyl), $-SO_2(C_1$ - C_4 alkyl), $-SO_2(C_1$ - C_4 alkyl), $-SO_2(C_1$ - C_4 alkyl), and $-SO_2N(C_1$ - C_4 alkyl) $(C_1$ - C_2 alkyl), $-SO_2(C_1$ - C_4 alkyl), $-SO_2(C_1$ - C_4 alkyl), $-SO_2(C_1$ - C_4 alkyl), $-SO_2(C_1$ - C_4 alkyl), and $-SO_2N(C_1$ - C_4 alkyl), $-SO_2(C_1$ - C_4 alkyl), $-SO_2(C_1$ - C_4 alkyl), and $-SO_2N(C_1$ - C_4 alkyl) $(C_1$ - C_2 alkyl);

-NR'R² or CR¹R²R¹⁰ may form a ring selected from saturated 3 to 8 membered rings, the 5 to 8 membered rings of which may optionally contain one or two double bonds, and wherein one or two of the ring carbon atoms of such 5 to 8 membered rings may optionally and independently be replaced by an oxygen or sulfur atom or by NZ² wherein Z² is hydrogen, benzyl or C₁-C₄ alkyl;

 R^3 is hydrogen, C_1 - C_4 alkyl, -O(C_1 - C_4 alkyl), chloro, fluoro, bromo, iodo, -S(C_1 - C_4 alkyl) or -SO₂(C_1 - C_4 alkyl);

each R^8 , R^9 and R^{12} is selected, independently, from hydrogen and C_1 - C_2 alkyl; each R^4 and R^6 that is attached to a carbon atom is selected, independently, from hydrogen and C_1 - C_6 alkyl, fluoro, chloro, bromo, iodo, hydroxy, hydroxy (C_1 - C_2 alkyl), trifluoromethyl, cyano, amino, nitro, - $O(C_1$ - C_4 alkyl), - $N(C_1$ - C_4 alkyl)(C_1 - C_2 alkyl), - C_2 alkyl), - C_3 - C_4 alkyl), - C_4 - C_5 - C_6 alkyl), wherein each of the C_1 - C_2 alkyl moieties in the foregoing R^4 and R^6 groups may optionally contain one double or triple bond; and R^6 , when attached to a nitrogen atom, is selected from hydrogen and C_1 - C_4 alkyl;

R⁵ is substituted phenyl, naphthyl, pyridyl or pyrimidyl, wherein each of the foregoing R⁵ groups is

substituted with from two to four substituents R^{13} , wherein up to three of said substituents may be selected, independently, from chloro, C_1 - C_6 alkyl, $-O(C_1$ - $C_{(3}$ alkyl) and $-(C_1$ - C_6 alkylene) $O(C_1$ - C_6 alkyl), and wherein one of said substituents may be selected, independently, from bromo, iodo, formyl, cyano, trifluoromethyl, nitro, amino, $-NH(C_1$ - C_4 alkyl), $-N(C_1$ - C_2 alkyl)(C_1 - C_6 alkyl), $-C(=O)O(C_1$ - C_4 alkyl), -OOOH, $-SO_2NH(C_1$ - C_4 alkyl), $-SO_2N(C_1$ - C_2 alkyl)(C_1 - C_4 alkyl), $-SO_2NH_2$, $-NHSO_2(C_1$ - C_4 alkyl), $-(C_0$ - C_1 alkylene)- $-S(C_1$ - $-C_2$ alkyl), $-(C_0$ - $-C_1$ alkylene)- $-SO_2$ - $-(C_1$ - $-C_2$ alkyl) and $-(C_1$ - $-C_4$ alkylene)--OH, and wherein each of the $-C_1$ - $-C_4$ alkyl and $-C_1$ - $-C_4$ alkyl moieties in the foregoing $-C_1$ 0 groups may optionally be substituted with one or two substituents independently selected from fluoro, hydroxy, amino, methylamino, dimethylamino and acetyl; $-C_1$ 1 shydrogen, methyl, halo (e.g., chloro, fluoro, iodo or bromo), hydroxy, methoxy, $-C(=O)(C_1$ - $-C_2$ alkyl), $-C(=O)O(C_1$ - $-C_2$ alkyl), hydroxymethyl, trifluoromethyl or formyl;

R¹⁰ is hydrogen, hydroxy, methoxy or fluoro; and

R¹¹ is hydrogen or C₁-C₄ alkyl;

with the proviso that in the ring containing D, E, K and G of formula I, there can not be two double bonds adjacent to each other;

and the pharmaceutically acceptable salt of such compound.

10. (Withdrawn) A pharmaceutical composition according to claim 1 wherein said corticotropin releasing factor antagonist is a compound of formula

$$R^4$$
 S N N N R^5 N N R^6

wherein each of R^1 and R^2 is independently a halogen atom; a C_1 - C_{15} hydroxyalkyl radical; C_1 - C_5 alkyl; C₁-C₁₀ aralkyl; C₁-C₅ alkoxy; trifluoromethyl; nitro; nitrile; a group - SR where R is hydrogen, a C₁-C₅ alkyl radical or a C₇-C₁₀ aralkyl radical; a group S-CO-R where R is a C₁-C₅ alkyl radical or aralkyl in which the aryl portion is C₆-C₈ and the alkyl portion is C₁-C₄; a group -COOR where R' is hydrogen or C₁-C₅ alkyl; a group -CONR'R" where R' and R" are as defined above for R'; a group -NR'R" where R' and R" are as previously defined for R'; a group -CONRaRb or NRaRb, where Ra and Rb, taken together with the nitrogen atom to which they are attached, form a 5- to 7membered heterocyclic ring; or a group -NHCO-NR'R", where R' and R" are as defined above for R'; R^3 is hydrogen or as defined for R' and R^2 is a hydrogen atom; C_{1-5} alkyl; halogen; a hydroxymethyl group; or a formyl group; R5 is C1-C5 alkyl; a C3-C7 cycloalkyl group; a cycloalkylalkyl group in which the cycloalkyl portion is C₃-C₇ and the alkyl portion is C₁-C₅; or C₅-C₆ alkenyl; n is O or 1; R⁶ is C₁-5 alkyl; alkoxyalkyl in which the alkyl portions are C₁-C₅; C₃-C₇ cycloalkyl; a cycloalkylalkyl group in which the cycloalkyl portion is C3-C7 and the alkyl portion is C₁-C₅; a cycloalkyloxyalkyl radical in which the cycloalkyl is C₃-C₇ and the alkyl is C₁-C₄; a USERS\DOCS\LA21952\LPAED\4k9y01!.DOC / 212902 - 24 -

hydroxyalkyloxyalkyl radical in which the alkyls are C_2 - C_{10} ; or an alkoxyalkyloxyalkyl radical in which the alkyls are C_3 - C_{12} ; and Z is an optionally substituted bi- or tricyclic aromatic or heteroaromatic group; and stereoisomers and/or addition salts thereof.

11. (Withdrawn) A pharmaceutical composition according to claim 1 wherein said corticotropin releasing factor antagonist is a compound of formula

$$R^3$$
 R^3
 R^2
 R^3
 R^2

including the stereoisomers and the pharmaceutically acceptable acid addition salt forms thereof, wherein

R¹ is NR⁴R⁵ or OR⁵;

R² is C₁-C₆alkyl, C₁-C₆alkyloxy or C₁-C₆alkylthio,

R³ is hydrogen, C₁-C₆alkyl, C₁-C₆alkylsulfonyl, C₁-C₆alkylsulfoxy or C₁-C₆alkylthio;

 R^4 is hydrogen, C_1 - C_6 alkyl, mono- or di(C_3 - C_6 cyloalkylmethyl, C_3 - C_6 cyloalkyl, C_3 - C_6 alkyl, hydroxy C_1 - C_6 alkyl, C_1 - C_6 alkyl,

 R^5 is C_1 - C_8 alkyl, mono- or $di(C_3$ - C_6 cycloalkyl)methyl, Ar^1CH_2 , C_3 - C_6 alkenyl, C_1 - C_6 alkyloxy C_1 - C_6 alkyl, hydroxy C_1 - C_6 alkyl, thienylmethyl, furanylmethyl, C_1 - C_6 alkylthio C_1 - C_6 alkyl, morpholinyl, mono- or $di(C_1$ - C_6 alkyl)amino C_1 - G_6 alkyl, $di(C_1$ - G_6 alkyl)amino, G_1 - G_6 alkyl, G_1 - G_6 alkyl, G_1 - G_6 alkyl substituted with imidazolyl; or a radical of formula -Alk-O-CO-Ar 1 ;

or R^4 and R^5 taken together with the nitrogen atom to which they are attached may form a pyrrolidinyl, piperidinyl, homopiperidinyl or morpholinyl group, optionally substituted with C_1 - C_6 alkyl or C_1 - C_6 alkyl, and

Ar is phenyl; phenyl substituted with 1, 2 or 3 substituents independently selected from halo, C_1 - C_6 alkyl, trifluoromethyl, hydroxy, cyano, C_1 - C_6 alkyloxy, benzyloxy, C_1 - C_6 alkylthio, nitro, amino and mono- or di(C_1 - C_6 alkyl)amino; pyridinyl; pyridinyl substituted with I ~ 2 or 3 substituents independently selected from halo, C_1 - C_6 alkyl, trifluoromethyl, hydroxy, cyano, C_1 - C_6 alkyloxy, benzyloxy, C_1 - C_6 alkylthio, nitro, amino, mono- or di(C_1 - C_6 alkyl)amino and piperidinyl; and wherein said substituted phenyl may optionally be further substituted with one or more halogens;

Ar¹ is phenyl; phenyl substituted with 1, 2 or 3 substituents each independently selected from halo, C_1 - C_6 alkyl, C_1 - C_6 alkyl, C_1 - C_6 alkyl)amino C_1 - C_6 alkyl, trifluoromethyl and C_1 - C_6 alkyl substituted with morpholinyl; or pyridinyl; and Alk is C_1 - C_6 alkanediyl;

with the proviso that 5-methyl-3-phenyl-7-(phenylmethoxy)-pyrazolo[1,5-a]-pyrimidine and 2,5-di methyl-7-(methylamino)-3-phenyl-pyrazolo[1,5-a]pyrimidine are not included.

12. (Withdrawn) A pharmaceutical composition according to claim 1 wherein said corticotropin releasing factor antagonist is a compound of formula

$$R^3$$
 R^1
 R^2

including the stereoisomers and the pharmaceutically acceptable acid addition salt forms thereof, wherein

X is S, SO or SO₂;

R¹ is NR⁴R⁵ or OR⁵:

R² is C₁-C₆alkyl, C₁-C₆alkyloxy or C₁-C₆alkylthio;

R³ is hydrogen, C₁-C₆alkyl, C₁-C₆alkylsulfonyl, C₁-C₆alkylsulfoxy or C₁-C₆alkylthio;

 R^4 is hydrogen, C_{1^-6} alkyl, mono- or di(C_3 - C_6 cycloalkyl)methyl, C_3 - C_6 cycloalkyl, C_3 - C_6 alkenyl,

 $hydroxyC_1-C_6alkyl,\ C_1-C_6alkylcarbonyloxyC_1-C_6alkyl\ or\ C_1-C_6alkyloxyC_1-C_6alkyl;$

 R^5 is C_1 - C_8 alkyl, mono- or $di(C_3$ - C_6 cycloalkyl)methyl, Ar^1CH_2 , C_3 - C_6 alkenyl, C_1 - C_6 alkyloxy C_1 - C_6 alkyl, hydroxy C_1 - C_6 alkyl, thienylmethyl, furanylmethyl, C_1 - C_6 alkylthio C_1 - C_6 alkyl, morpholinyl, mono- or $di(C_1$ - C_6 alkyl)amino C_1 - C_6 alkyl, $di(C_1$ - C_6 alkyl)amino, C_1 - C_6 alkylcarbonyl C_1 - C_6 alkyl, C_1 - C_6 alkyl substituted with imidazolyl; or a radical of formula -Alk-O-CO-Ar I;

or R^4 and R^5 taken together with the nitrogen atom to which they are attached may form a pyrrolidinyl, piperidinyl, homopiperidinyl or morpholinyl group, optionally substituted with C_1 - C_6 alkyl or C_1 - C_6 alkyloxy C_1 - C_6 alkyl;

Ar is phenyl; phenyl substituted with 1, 2 or 3 substituents independently selected from halo, C_1 - C_6 alkyl, trifluoromethyl, hydroxy, cyano, C_1 - C_6 alkyloxy, benzyloxy, C_1 - C_6 alkylthio, nitro, amino and mono- or di(C_1 - C_6 alkyl)amino; pyridinyl; pyridinyl substituted with 1, 2 or 3 substituents independently selected from halo, C_1 - C_6 alkyl, trifluoromethyl, hydroxy, cyano, C_1 - C_6 alkyloxy, benzyloxy, C_1 - C_6 alkylthio, nitro, amino, mono- or di(C_1 - C_6 alkyl)amino and piperidinyl; and wherein said substituted phenyl may optionally be further substituted with one or more halogens;

 Ar^{1} is phenyl; phenyl substituted with 1, 2 or 3 substituents each independently selected from halo, C_{1} - C_{6} alkyl, C_{1} - C_{6} alkyloxy, di(C_{1} - C_{6} alkyl)amino C_{1} - C_{6} alkyl trifluoromethyl, and C_{1} - C_{6} alkyl substituted with morpholinyl; or pyridinyl; and Alk is C_{1} - C_{6} alkanediyl.

13. (Currently amended) A pharmaceutical composition according to claim 4 <u>4</u> wherein said corticotropin releasing factor antagonist is a compound selected from the group consisting of: 4-(1-ethyl-propoxy)-3,6-dimethyl-2-(2,4,6-trimethylphenoxy)-pyridine;

butyl-[2,5-dimethyl-7-(2,4,6-trimethylphenyl)-6,7-dihydro-5H-pyrrolo[2,3d]pyrimidin-4-yl]-ethyl-amine; 4-(butyl-ethylamino)-2,5-dimethyl-7-(2,4,6-trimethylphenyl)-5,7-dihydropyrrolo[2,3-d]pyrimidin-6-one;

4-(1-ethylpropoxy)-2,5-dimethyl-6-(2,4,6-trimethylphenoxy)-pyrimidine;

N-butyl-N-ethyl-2,5-dimethyl-NN-(2,4,6-trimethylphenyl)-pyrimidine-4,6diamine;

[4-(1-ethyl-propoxy)-3,6-dimethyl-pyridin-2-yl]-(2,4,6-trimethylphenyl)-amine;

6-(ethyl-propyl-amino)-2,7-dimethyl-9-(2,4,6-trimethylphenyl)-7,9-dihydropurin-8-one;

3-{(4-methyl-benzyl)-[3,6-dimethyl-1-(2,4,6-trimethylphenyl)-1-H-pyrazolo[3,4d]pyrimidin-4-yl]-amine}propan-1-ol;

diethyl-[6-methyl-3-methylsulfanyl-1-(2,4,6-trichlorophenyl)-1 H-pyrazolo[3,4d]pyrimidin-4-yl]-amine; 2-{butyl-[6-methyl-3-methylsulfanyl-1-(2,4,6-trichlorophenyl)-1 H-pyrazolo[3,4d]pyrimidin-4-yl]-amino}ethanol;

dibutyl-[6-methyl-3-methylsulfanyl-1-(2,4,6-trichlorophenyl)-1 H-pyrazolo[3,4-d]pyrimidin-4-yl}-amine; butyl-ethyl-[6-methyl-3-methylsulfanyl-1-(2,4,6-trichlorophenyl)-1H-pyrazolo[3,4-d]pyrimidin-4-yl]-amine;

butyl-ethyl-[6-methyl-3-methylsulfanyl-1-(2,4,6-trichlorophenyl)-1-H-pyrazolo[3,4-d]pyrimidin-4-yl]-amine:

butyl-cyclopropylmethyl-[6-methyl-3-methylsulfanyl-1-(2,4,6-trichlorophenyl)1-H-pyrazolo[3,4-d]pyrimidin-4-yl]-amine;

di-1-propyl-[6-methyl-3-methylsulfanyl-1-(2,4,6-trichlorophenyl)-1-H-pyrazolo[3,4-d]pyrimidin-4-yl]-amine;

diallyl-[6-methyl-3-methylsulfanyl-1-(2,4,6-trichlorophenyl)-1-H-pyrazolo[3,4-d]pyrimidin-4-yl]-amine; butyl-ethyl-[6-chloro-3-methylsulfanyl-1-(2,4,6-trichlorophenyl)-1-H-pyrazolo[3,4-d]pyrimidin-4-yl]-amine:

butyl-ethyl-[6-methoxy-3-methylsulfanyl-1-(2,4,6-trichlorophenyl)-1-H-pyrazolo[3,4-d]pyrimidin-4-yl]-amine:

propyl-othyl-[3,6-dimothyl-1-(2,4,6-trimothylphonyl)-1 H-pyrazolo[3,4-d]pyrimidin-4-yl]-amine;
4-(1-othyl-propyl)-6-methyl-3-methylsulfanyl-1-(2,4,6-trimothylphonyl)-1 H-pyrazolo[3,4-d]pyrimidine;
n-butyl-othyl-[2,5-dimothyl-7-(2,4,6-trimothylphonyl)-7H-pyrrolo[2,3-d]pyrimidin-4-yl]amine;
di-n-propyl-[2,5-dimothyl-7-(2,4,6-trimothylphonyl)-7H-pyrrolo[2,3-d]pyrimidin-4-yl]amine;
othyl-n-propyl-[2,5-dimothyl-7-(2,4,6-trimothylphonyl)-7H-pyrrolo[2,3-d]pyrimidin-4-yl]amine;
diothyl-2,5-dimothyl-7-(2,4,6-trimothylphonyl)-7H-pyrrolo[2,3-d]pyrimidin-4-yl]amine;
n-butyl-othyl-[2,5,6-trimothyl-7-(2,4,6-trimothylphonyl)-7H-pyrrolo[2,3-d]pyrimidin-4-yl]amine;
2-{N-n-butyl-N-[2,5-dimothyl-7-(2,4,6-trimothylphonyl)-7H-pyrrolo[2,3-d]pyrimidin-4-yl]amino}-othanol;

4-(1-ethyl-propyl)-2,5,6-trimethyl-7-(2,4,6-trimethylphenyl)-7H-pyrrolo[2,3-d]pyrimidine; n-butyl-ethyl-[2,5-dimethyl-7-(2,4-dimethylphenyl)-7H-pyrrolo[2,3-d]pyrimidin-4-yl]amine; 2,5-dimethyl-7-(2,4,6-trimethylphenyl)-7H-pyrrolo[2,3-d]pyrimidyl-4-yl]-(1-ethyl-propyl)amine; butyl-[3,6-dimethyl-1-(2,4,6-trimethylphenyl)-1-H-pyrazolo[3,4-b]pyridin-4-yl]-ethylamine; [3,6-dimethyl-1-(2,4,6-trimethylphenyl)-1-H-pyrazolo[3,4,b]pyridin-4-yl]-(1-methoxymethylpropyl)-amine;

4-(1-methoxymethylpropoxy)-3,6-dimethyl-1-(2,4,6-trimethylphonyl)-1-H-pyrazolo[3,4-b]pyridine; (1-ethyl propyl)-[3,5,6-trimethyl-1-(2,4,6-trimethylphonyl)-1-H-pyrazolo[3,4-b]pyridin-4-yl]-amine; 4-(1-ethylpropoxy)-2,5-dimethyl-7-(2,4,6-trimethylphonyl)-7H-pyrrolo[2,3-b]pyridine; 4-(1-ethylpropoxy)-2,5,6-trimethyl-7-(2,4,6-trimethylphonyl)-7H-pyrrolo[2,3-b]pyridine; 4-(1-ethyl-propoxy)-2,5-dimethyl-7-(2,6-dimethyl-4-bromop-he-nyl)-7H-pyrrolo[2,3-b]pyridine;

- 2,5,6-trimethyl-7-(1-propylbutyl)-4-(2,4,6-trimethylphenoxy)-7H-pyrrolo[2,3-d]pyrimidine; 1-(1-ethyl propyl)-6-methyl-4-(2,4,6-trimethyl phenylamino)-1,3-dihydro-imidazol4,5-clpyridin-2one: 9-(1-ethylpropyl)-2-methyl-6-(2,4,6-trimethylphenylamino)-7,9-dihydro-purin-8-one; 1-(1-ethylpropyl)-6-methyl-4-(2,4,6-trimethylphonoxy)-1,3-dihydro-imidazo[4,5-c]pyridin-2-one; 1-(1-ethyl propyl)-6-methyl-4-(2,4,6-trimethyl phenoxy)-1 H-imidazo[4,5-c]pyridine; 1-(1-ethylpropyl)-3,6-dimethyl-4-(2,4,6-trimethylphenoxy)-1,3-dihydro-imidazo[4,5-c]pyridin-2ono;
- 1-(1-ethylpropyl)-3,6-dimethyl-4-(2,4,6-trimethylphenylamino)-1,3-dihydro-imidazo[4,5-c]pyridin-
- 1-(1-ethyl-propyl)-4,7-dimethyl-5 (2,4,6-trimethyl-phenoxy)-1,4-dihydro-2H-pyrido[3,4-b]pyrazin-3-one;
- 1-(1-ethyl-propyl)-4,7-dimethyl-5-(2,4,6-trimethyl-phenoxy)-1,2,3,4-tetrahydro-pyrido[3,4-b]pyrazine;
- 1-(1-ethyl-propyl)-7-methyl-5-(2,4,6-trimethyl-phenoxy)-1,2,3,4-tetrahydro-pyrido[3,4-b]pyrazine;
- 1-(1-ethyl-propyl)-7-methyl-2-oxo-5-(2,4,6-trimethyl-phonoxy)-1,2,3,4-tetra-hydro-[1,6]naphthyridine-3carboxylic acid methyl-ester;
- 1-(1-ethyl-propyl) 7-methyl-2-exe-5-(2,4,6-trimethyl-phenexy) 1,2,3,4-tetra-hydro-[1,6]naphthyridine-3carboxylic acid-isopropyl ester:
- 1-(1-ethyl-propyl) 7-methyl-5-(2,4,6-trimethyl-phenoxy) 3,4-dihydro-1 H-[1,6]naphthyridin-2-one;
- 1-(1-ethyl-propyl)-7-methyl-5-(2,4,6-trimethyl-phenoxy)-1,2,3,4-tetrahydro[1,6]naphthyridine;
- 15 1-(1-ethyl-propyl)-7-methyl-5-(2,4,6-trimethyl-phenoxy)-1,4-dihydro-2H-3oxa-1,6-diazanaphthalene;
- 1-(1-ethyl-propyl)-4,7-dimethyl-5-(2,4,6-trimethyl-phenoxy)-1,4-dihydro-2H3-oxa-1,6-diazanaphthalene;
- 1-(1-ethyl-propyl) 3,7-dimethyl-5-(2,4,6-trimethyl-phenoxy) 3,4-dihydro1 H-3-oxa-[1,6]-naphthyridin-2ene:
- 1-(1-ethyl-propyl)-3,3,6-trimethyl-4-(2,4,6-trimethyl-phenoxy)-2,3-dihydro1 H-pyrrolo[3,2-c]pyridine;
- 7-(1-ethyl-propoxy)-5-methyl-3-(2,4,6-trimethyl-phenyl)-pyrazolo[1,5a]pyrimidine;
- [2,5-dimethyl-3-(2,4,6-trimethyl-phenyl)-pyrazolo[1,5-a]pyrimidin-7-yi]-(1-ethylpropyl)-amine;
- (1-ethyl-propyl)-[5-methyl-3-(2,4,6-trimethyl-phenyl)-pyrazolo[1,5-a]pyrimidin7-yl]-amine;
- 7-(1-ethyl-propoxy)-2,5-dimethyl-3-(2,4,6-trimethyl-phenyl)-pyrazolo[1,5-a]pyrimidine;
- [2,5-dimethyl-3-(2,4,6-trimethyl-phenyl)-pyrazolo[1,5-a]pyrimidin-7-yl]-ethylpropyl-amine;
- [6-bromo-5-bromomethyl-3-(2,4,6-trimethyl-phenyl)-3H-[1,2,3]triazolo[4,5b]pyridin-7-yl]-(1-ethylpropyl)-amine;
- (1-ethyl-propyl)-[5-methyl-3-(2,4,6-trimethyl-phenyl)-3H-[1,2,3]triazolo[4,5b]pyridin-7-yl]-amine; [6-bromo-5-methyl-3-(2,4,6-trimethyl-phonyl)-3H-[1,2,3]triazolo[4,5-b]pyridin7-yl]-(1-ethyl-propyl)methyl-amine;
- 7-(1-ethyl-propoxy)-5-methyl-3-(2,4,6-trimethyl-phenyl)-3H-[1,2,3]triazolo[4,5b]pyridine; 4-(1-ethyl-propoxy)-2,5-dimethyl-7-(2,4,6-trimethyl-phenyl)-5H-pyrrolo[3,2d]pyrimidine;

- (+)-2,5-dimethyl-4-(tetrahydro-furan-3-yloxy)-7-(2,4,6-trimethyl-phonyl)-5H-pyrrolo-[3,2-d]pyrimidine;
- 2,5-dimethyl-4-(S)-(tetrahydro-furan-3-yloxy)-7-(2,4,6-trimethyl-phonyl)-5Hpyrrolo-[3,2-d]pyrimidine;
- 2,5-dimethyl-4-(1-propyl-butoxy)-7-(2,4,6-trimethyl-phonyl)-5H-pyrrolo[3,2d]pyrimidine;
- 4-sec-butylsulfanyl-2,5-dimethyl-7-(2,4,6-trimethyl-phenyl)-5H-pyrrolo[3,2d]pyrimidine;
- 4-(butyl-ethyl-amine)-2,6-dimethyl-8-(2,4,6-trimethyl-phenyl)-5,8-dihydro-6Hpyrido[2,3-d]pyrimidin-7-one;
- 8-(1-ethyl-propoxy)-6-methyl-4-(2,4,6-trimethyl-phenyl)-3,4-dihydro-1 H-pyrido[2,3-b] pyrazin-2-one;
- 8-(1-ethyl-propoxy)-6-methyl-4-(2,4,6-trimethyl-phenyl)-1,2,3,4-tetrahydropyrido [2,3-b]pyrazine;
- 4-(1-ethyl-propoxy)-2-methyl-8-(2,4,6-trimethyl-phenyl)-quinoline; 5-(1-ethyl-propoxy)-7-methyl-
- 1-(2,4,6-trimethyl-phenyl)-1,4-dihydro-2H-3-oxa-1,8-diaza-naphthalene;
- 5-(1-ethyl-propoxy)-7-methyl-1-(2,4,6-trimethyl-phonyl)-1,2-dihydro-3-oxa-1,8diaza-naphthalen-4-one;
- 8-(1-ethyl-propoxy)-1,6-dimethyl-4-(2,4,6-trimethyl-phonyl)-1,2,3,4tetrahydro-pyrido[2,3-b]pyrazine;
- (1-ethyl-propyl)-[2-methyl-8-(2,4,6-trimethyl-phonyl)-quinol in-4-yl]-amine;
- 4-(butyl-ethyl-amino)-2,6-dimethyl-8-(2,6-dimethyl-4-bromo-phenyl)-5,8dihydro-6H-pyrido[2,3-d]pyrimidin-7-one;
- 4-(butyl-ethyl-amino)-2-methyl-8-(2,6-dimethyl-4-bromo-phenyl)-5,8-dihydro-6 H-pyrido[2,3-d]pyrimidin-7-one;
- 4-(1-ethyl-propoxy)-2-methyl-8-(2,6-dimethyl-4-bromo-phonyl)-5,8-dihydro-6Hpyrido[2,3-d]pyrimidin-7-one:
- (butyl-ethyl)-[2-methyl-8-(2,6-dimethyl-4-bromo-phenyl)-5,6,7,8-tetrahydropyrido[2,3-d]pyrimidin-4-yl]-amine:
- (propyl-ethyl)-[2-methyl-8-(2,6-dimethyl-4-bromo-phenyl)-5,6,7,8-tetrahydropyrido[2,3-d]pyrimidin-4-yl]-amine;
- (diethyl)-[2-methyl-8-(2,6-dimethyl-4-bromo-phonyl)-5,6,7,8-tetrahydropyrido [2,3-d]pyrimidin-4-yl]-amine;
- (1-ethyl-propyl)-[2-methyl-8-(2,6-dimethyl-4-bromo-phenyl)-5,6,7,8-tetrahydro-pyrido[2,3-d]pyrimidin-4-yl]-amine;
- (1-ethyl-propoxy)-2-methyl-8-(2,6-dimethyl-4-bromo-phenyl)-5,6,7,8tetrahydro-pyrido[2,3-d]pyrimidine;
- 4-(butyl-ethyl-amino)-2-methyl-8-(2,4,6-trimethyl-phenyl)-5,8-dihydro-6Hpyrido[2,3-d]pyrimidin-7-one; 4-(1-ethyl-propoxy)-2-methyl-8-(2,4,6-trimethyl-phenyl)-5,8-dihydro-6Hpyrido [2,3-d]pyrimidin-7-one; (butyl-ethyl)-[2-methyl-8-(2,4,6-trimethyl-phenyl)-5,6,7,8-tetrahydro-pyrido[2,3d] pyrimidin-4-yl]-amino; (propyl-ethyl)-[2-methyl-8-(2,4,6-trimethyl-phenyl)-5,6,7,8-tetrahydro-pyrido-[2,3-d] pyrimidin-4-yl]-

amine;

(diethyl) [2-methyl-8-(2,4,6-trimethyl-phenyl) 5,6,7,8-tetrahydro-pyrido[2,3-d] pyrimidin-4-yl]-amine; (1-ethyl-propyl) [2-methyl-8-(2,4,6-trimethyl-phenyl) 5,6,7,8-tetrahydropyrido[2,3-d] pyrimidin-4-yl]-amine;

(1-ethyl-propoxy)-2-methyl-8-(2,4,6-trimethyl-phonyl)-5,6,7,8-tetrahydropyrido[2,3-d] pyrimidine; 8-(1-ethyl-propoxy)-6-methyl-4-(2,6-dimethyl-4-brome-phonyl)-3,4-dihydro1-H-pyrido [2,3-b]pyrazin-2-one;

8-(1-ethyl-propoxy)-6-methyl-4-(2,6-dimethyl-4-bromo-phenyl)-1,2,3,4-tetrahydro-pyrido[2,3-b]pyrazine;

4-(1-ethyl-propoxy)-2-methyl-8-(2,6-dimethyl-4-bromo-phenyl)-q-uinoline;

5-(1-ethyl-propoxy)-7-methyl-1-(2,6-dimethyl-4-bromo-phenyl)-1,4-dihydro-2H3-oxa-1,8-diaza-naphthalene;

5-(1-ethyl-propoxy)-7-methyl-1-(2,6-dimethyl-4-bromo-phenyl)-1,2-dihydro-3exa-1,8-diaza-naphthalen-4-one;

8-(1-ethyl-propoxy)-1,6-dimethyl-4-(2,6-dimethyl-4-brome-phenyl)-1,2,3,4tetrahydro-pyride[2,3-b]pyrazine;

5 (1-ethyl-propyl)-[2-methyl-8-(2,6-dimethyl-4-bromo-phenyl)-quinolin-4-yl]amine;

4-(butyl-ethyl-amino)-2,6-dimethyl-8-(2,6-dimethyl-4-chloro-phonyl)-5,8dihydro-6H-pyrido[2,3-d]pyrimidin-7-one;

8-(1-ethyl-propoxy)-6-methyl-4-(2,6-dimethyl-4-chloro-phenyl)-3,4-dihydro-1-H-pyrido[2,3-b]pyrazin-2-one;

8-(1-ethyl-propoxy)-6-methyl-4-(2,6-dimethyl-4-chloro-phenyl)-1,2,3,4tetrahydro-pyrido[2,3-b]pyrazine;

4-(1-ethyl-propoxy)-2-methyl-8-(2,6-dimethyl-4-chloro-phenyl)-quinoline;

5-(1-ethyl-propoxy)-7-methyl-1-(2,6-dimethyl-4-chloro-phenyl)-1,4-dihydro-2H-3-oxa-1,8-diaza-naphthalene;

5-(1-ethyl-propoxy)-7-methyl-1-(2,6-dimethyl-4-chloro-phonyl)-1,2-dihydro-3oxa-1,8-diaza-naphthalen-4-one;

8-(1-ethyl-propoxy)-1,6-dimethyl-4-(2,6-dimethyl-4-chloro-phenyl)-1,2,3,4tetrahydro-pyrido[2,3-b]pyrazine;

(1-ethyl-propyl) [2-methyl-8-(2,6-dimethyl-4-chloro-phenyl) quinolin-4-yl]amine;

8-(1-hydroxymethyl-propoxy) 6-methyl-4-(2,4,6-trimethyl-phenyl) 3,4-dihydro1 H-pyrido[2,3-b]pyrazin-2-one;

8-(1-hydroxymethyl-propylamino)-6-methyl-4-(2,4,6-trimethyl-phenyl)-3,4-dihydro-1-H-pyrido[2,3-b]pyrazin-2-one;

8-(1-ethyl-propylamino)-6-methyl-4-(2,4,6-trimethyl-phenyl)-3,4-dihydro-1-Hpyrido[2,3-b]pyrazin-2-one; 8-diethylamino-6-methyl-4-(2,4,6-trimethyl-phenyl)-3,4-dihydro-1-H-pyrido[2,3-b] pyrazin-2-one; 8-(ethyl-propyl-amino)-6-methyl-4-(2,4,6-trimethyl-phenyl)-3,4-dihydro-1-Hpyrido[2,3-b]pyrazin-2-one;

- 8-(butyl-ethyl-amino) 6-methyl-4-(2,4,6-trimethyl-phenyl) 3,4-dihydro-1 Hpyride [2,3-b]pyrazin-2-one; 8-(1-hydroxymethyl-propoxy)-6-methyl-4-(2,4,6-trimethyl-phenyl)-1,2,3,4tetrahydro-pyrido[2,3-b]pyrazine;
- 8-(1-hydroxymethyl-propylamino) 6-methyl-4-(2,4,6-trimethyl-phenyl)-1,2,3,4tetrahydro-pyrido[2,3-b]pyrazine;
- 5 8-(1-ethyl-propylamino)-6-methyl-4-(2,4,6-trimethyl-phonyl)-1,2,3,4tetrahydro-pyrido[2,3-b]pyrazine;
- 8-diethylamino-6-methyl-4-(2,4,6-trimethyl-phenyl)-1,2,3,4-tetrahydropyrido[2,3-b]pyrazine;
- 8-(ethyl-propyl-amino)-6-methyl-4-(2,4,6-trimethyl-phonyl)-1,2,3,4-tetrahydro-pyrido[2,3-b]pyrazine;
- 8-(butyl-ethyl-amino)-6-methyl-4-(2,4,6-trimethyl-phenyl)-1,2,3,4-tetrahydropyrido[2,3-b]pyrazine;
- 4-(1-hydroxymethyl-propoxy)-2-methyl-8-(2,4,6-trimethyl-phenyl)-quinoline;
- 4-(1-hydroxymethyl-propylamino)-2-methyl-8-(2,4,6-trimethyl-phenyl)-quinoline;
- 4-(1-ethyl-propylamino)-2-methyl-8-(2,4,6-trimethyl-phenyl)-quinoline;
- 4-diethylamino-2-methyl-8-(2,4,6-trimethyl-phenyl)-quinoline;
- 4-(ethyl-propyl-amino)-2-methyl-8-(2,4,6-trimethyl-phenyl)-quinoline;
- 4-(butyl-ethyl-amino)-2-methyl-8-(2,4,6-trimethyl-phenyl)-quinoline;
- 5-(1-hydroxymethyl-propoxy)-7-methyl-1-(2,4,6-trimethyl-phenyl)-1,4-dihydro2H-3-oxa-1,8-diazanaphthalene;
- 5-(1-hydroxymethyl-propylamino)-7-methyl-1-(2,4,6-trimethyl-phenyl)-1,4dihydro-2H-3-oxa-1,8diaza-naphthalene;
- 5-(1-ethyl-propylamino)-7-methyl-1-(2,4,6-trimethyl-phenyl)-1,4-dihydro-2H-3-oxa-1,8-diaza-naphthalene:
- 5-diethylamino-5-methyl-1-(2,4,6-trimethyl-phenyl)-1,4-dihydro-2H-3-oxa-1,8diaza-naphthalene; 5-(ethyl-propyl-amino)-7-methyl-1-(2,4,6-trimethyl-phenyl)-1,4-dihydro-2H-3oxa-1,8-diaza-naphthalene;
- 8-(butyl-ethyl-amino)-6-methyl-4-(2,4,6-trimethyl-phenyl)-1,4-dihydro-2H-3oxa-1,8-diaza-naphthalene;
- 4-(2,4-dichlorophenyl)-5-methyl-2-[N-(1-(methoxymethyl)-1-(naphth-2-yl) methyl)-N-propylamino]thiazole;
- exalate of 4-(2,4-dichlorophenyl)-5-methyl-2-[N-(6-methoxyisoquinol-5-yl)-Npropylamino]thiazole; exalate of 4-(2-chloro-4-methoxyphenyl)-5-methyl-2-[N-(6-methylisoquinol-5-yl)-N-propylamino]thiazole;
- 4-(2-chloro-4-methoxyphenyl) 5-methyl-2-[N-(1-methoxycarbonylmethylindol5-yl)-N-propylamino]thiazole;
- exalate of 4-(2-chlore-4-methoxyphenyl)-5-methyl-2-[N-(6-methoxyisoquinel5-yl)-N-propylamine]thiazele;
- oxalate of 4-(2-chloro-4-methoxyphenyl)-5-methyl-2-[N-(6-chloroisoquinol-5-yl)-N-

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propylamino]thiazolo;
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exalate of 4-(2-chlore-4-methoxyphenyl) 5-methyl-2-[N-(6-methoxyisoquinel-5-yl)-N-propylaminelthiazole:

4-(2-chloro-4-methoxyphenyl)-5-methyl-2-[N1-methoxynaphth-2-yl)-N-propylamino]thiazole; exalate of 4-(2-chloro-4-trifluoromethylphenyl)-5-methyl-2-[N-6methoxyisoquinol-5-yl)-N-propylamino]thiazole;

chlorhydrate of 4-(2-chloro-4-methoxyphonyl)-5-methyl-2-[N-(2ethoxynaphth-1-yl)-N-propylamino]thiazole;

ehlorhydrate of 4-(2-chloro-4-methoxyphenyl)-5-methyl-2[N-(2,3-dimethylnaphth-1-yl)-N-propylamino]thiazole;

chlorhydrate of 4-(2-chloro-4-methoxyphenyl)-5-methyl-2-[N-(6-bromo-2methoxynaphth-1-yl)-N-propylaminolthiazole;

chlorhydrate of 4-(2-chloro-4-methoxyphenyl)-5-methyl-2-[N-(2,6dimethylnaphth-1-yl)-N-propylamino]thiazole;

chlorhydrate of 4-(2-chloro-4-methoxyphenyl)-5-methyl-2-[N-(1(methoxymethyl)-1-(naphth-2-yl)methyl)-N-propylamino]thiazole;

chlorhydrate of 4-(2-chloro-4-methoxyphenyl)-5-methyl-2-[N-(1-(cyclopropyl)1-(naphth-2-yl)methyl)-N-propylamino]thiazole;

3-(2,4-dichlorophenyl)-5-methyl-7(N-propyl-N-cyclopropanemethylamino)3O-pyrazolo[2,3-a]pyrimidine;

3-(2,4-dichlorophenyl)-5-methyl-7-(N-allyl-N-cyclopropanemethylamino)pyrazolo[2,3-a]pyrimidine;

2-methylthio-3-(2,4-dichlorophenyl)-5-methyl-7-(N,N-diallylamino)pyrazolo[2,3-a]pyrimidine;

2-methylthio-3-(2,4-dichlorophenyl)-5-methyl-7-(N-butyl-N-cyclopropanemethyl-amino)pyrazolo[2,3-a]pyrimidine;

2-methylthio-3-(2,4-dichlorophenyl)-5-methyl-7-(N-propyl-N-cyclopropanemethyl-amino)pyrazolo[2,3-a]pyrimidine;

2-methyl-3-(4-chlorophenyl)-5-methyl-7-(N,N-dipropylamino)-pyrazolo[2,3-a] pyrimidine;

3-[6-(dimethylamino)-3-pyridinyl-2,5-dimethyl-N,N-dipropylpyrazolo[2,3-a] pyrimidin-7-amine;

3-[6-(dimethylamino)-4-methyl-3-pyridinyl]-2,5-dimethyl-N,N-dipropyl-pyrazolo[2,3-a]pyrimidine-7-amine;

3-(2,4-dimethoxyphenyl)-2,5-dimethyl-7-(N-propyl-N-methyloxyethylamino)pyrazolo(2,3-a)pyrimidine;

7-(N-diethylamino)-2,5-dimethyl-3-(2-methyl-4-methoxyphonyl-[1,5-a]pyrazolopyrimidine;

7-(N-(3-cyanopropyl) N-propylamino-2,5,dimethyl-3-(2,4-dimethylphenyl) [1,5a]-pyrazolopyrimidine;

[3,6-dimethyl-2-(2,4,6-trimethyl-phenoxy)-pyridin-4-yl]-(1-ethyl-propyl)-amine;

[2-(4-chloro-2,6-dimethyl-phenoxy)-3,6-dimethyl-pyridin-4-yl]-(1-ethyl-propyl)-amine;

cyclopropylmothyl-[3-(2,4-dimethyl-phenyl)-2,5-dimethyl-pyrazolo[1,5a]pyrimidin-7-yl]-propyl-amine; cyclopropylmothyl-[3-(2-methyl-4-chloro-phonyl)-2,5-dimethyl-pyrazolo[1,5a]pyrimidin-7-yl]-propyl-amine;

cyclopropylmethyl-[3-(2,4-di-chloro-phenyl)-2,5-dimethyl-pyrazolo[1,5-a]pyrimidin-7-yl]-propyl-amine; [3-(2-methyl-4-chloro-phenyl)-2,5-dimethyl-pyrazolo[1,5-a]pyrimidin-7-yl]-di-propyl-amine; [2,5-dimethyl-3-(2,4-dimethyl-phenyl)-pyrazolo[1,5-a]pyrimidin-7-yl]-(1-ethylpropyl)-amine; [2,5-dimethyl-3-(2,4-dichloro-phenyl)-pyrazolo[1,5-a]pyrimidin-7-yl]-(1-ethylpropyl)-amine; 4-(1-ethyl-propylamino)-6-methyl-2-(2,4,6-trimethyl-phenoxy)-nicotinic acid methyl ester; 3-[6-(dimethylami-no)-4-methyl-3-pyridinyl]-2,5-dimethyl-N-propyl-Ncyclopropylmethyl-pyrazolo[2,3-a]pyrimidin-7-amine; and 3-[6-(dimethylamino)-4-methyl-3-pyridinyl]-2,5-dimethyl-N-ethyl-Ncyclopropylmethyl-pyrazolo[2,3-a]pyrimidin-7-amine,

wherein said growth hormone secretagogue is a compound of formula IV:

or a stereoisomeric mixture thereof, a diastereomerically enriched, diastereomerically pure, enantiomerically enriched, or enantiomerically pure isomer thereof, or a prodrug of such compound, mixture, or isomer thereof, or a pharmaceutically acceptable salt of the compound, mixture, isomer, or prodrug, wherein:

HET is a heterocyclic moiety selected from the group consisting of

d is O, 1, or 2;

e is 1 or 2;

f is O or 1;

n and w are O, 1, or 2, provided that n and w cannot both be O at the same time;

Y² is oxygen or sulfur;

A is a divalent radical, wherein the left hand side of the radical as shown below is connected to C" and the right hand side of the radical as shown below is connected to C', selected from the group consisting of $-NR^2$ -CO- NR^2 -, $-NR^2$ -SO₂- NR^2 -, -O-CO- NR^2 -, $-NR^2$ -CO₂-, -CO- NR^2 -CO-, -CO- NR^2 -CO-, $-C(R^9R^{10})$ -, $-C(R^9R^{$

 $\frac{C(R^9R^{10})_{-,} \cdot NR^2 \cdot C(R^{11}) = N \cdot CO - \cdot C(R^9R^{10}) - C(R^9R^{10}) - N(R^{12}) - C(R^9R^{10}) - NR^{12}_{-,} \cdot N = C(R^1) - NR^2 \cdot CO_{-,} - C(R^9R^{10}) -$

Q is a covalent bond or CH2; W is CH or N;

X is CR⁹R¹⁰, C=CH₂, or C=O; Y is CR⁹R¹⁰, O, or NR²;

Z is C=O, C=S, or SO₂;

 G^1 is hydrogen, halo, hydroxy, nitro, amino, cyano, phenyl, carboxyl, -CONH₂, -C₁-C₄ alkyl optionally independently substituted with one or more phenyl, one or more halogen, or one or more hydroxy groups, -C₁-C₄ alkoxy optionally independently substituted with one or more phenyl, one or more halogen, or one or more hydroxy groups, -C₁-C₄ alkylthio, phenoxy, -CO₂-(C₁-C₄ alkyl), N,N-di-(C₁-C₄ alkylamino), -C₂-C₆ alkenyl optionally independently substituted with one or more phenyl, one or more halogen, or one or more hydroxy groups, -C₂-C₆ alkynyl optionally independently substituted with one or more phenyl, one or more halogen, or one or more hydroxy groups, -C₃-C₆ cycloalkyl optionally independently substituted with one or more C₁-C₄ alkyl groups, one or more halogen, or one or more hydroxy groups, -C₁-C₄ alkylamino carbonyl, or di-C₁-C₄ alkylamino) carbonyl;

G² and G³ are each independently selected from the group consisting of hydrogen, halo, hydroxy, -C₁-C₄ alkyl optionally independently substituted with one to three halo groups, and -C₁-C₄ alkoxy optionally independently substituted with one to three halo groups;

 $\begin{array}{l} R^{1} \text{ is hydrogen, -CN, -(CH_{2})_{q}NX^{6}COX^{6}, -(CH_{2})_{q}NX^{6}CO(CH_{2})_{t}-A^{1} -(CH_{2})_{q}NX^{6}SO_{2}(CH_{2})_{t}-A^{1}, -(CH_{2})_{q}NX^{6}SO_{2}X^{6}, -(CH_{2})_{q}NX^{6}CONX^{6}(CH_{2})_{t}A^{1}, -(CH_{2})_{q}NX^{6}CONX^{6}X^{6}, -(CH_{2})_{q}CONX^{1}X^{6}, -(CH_{2})_{q}CONX^{1}X^{6}, -(CH_{2})_{q}COX^{1}X^{6}, -(CH_{2})_{q}COX^{1}X^{1}, -($

wherein the alkyl and cycloalkyl groups in the definition of R' are optionally substituted with C_1 - C_4 alkyl, hydroxy, C_1 - C_4 alkoxy, carboxyl, - CONH₂, -SO_m (C_1 - C_6 alkyl), -CO₂-(C_1 - C_4 alkyl) ester, 1 H-tetrazol-5-yl, or 1, 2, or 3 fluoro groups;

Y' is O, SO_m , $-CONX^6$ -, -CH=CH-, -C=C-, $-NX^6CO$ -, $-CONX^6$ -, $-CO_2$ -, $-OCONX^6$ - or -OCO-; q is O, 1, 2, 3, or 4; t is O, 1, 2, or 3;

said (CH2)g group and (CHA group in the definition of R' are optionally independently substituted with hydroxy, C_1 - C_4 alkoxy, carboxyl, -CONH₂, -SO, $(C_1$ - C_6 alkyl), -CO₂- $(C_1$ - C_4 alkyl) ester, 1 H-tetrazol-5-yl, 1, 2, or 3 fluoro groups, or 1 or 2 C_1 - C_4 alkyl groups;

 R^{1A} is selected from the group consisting of hydrogen, F, Cl, Br, I, C_1 - C_6 alkyl, phenyl- $(C_1$ - C_3 alkyl), provided that R^{1A} is not F, Cl, Br, or I when a heteroatom is vicinal to C'';

R² is hydrogen, C₁-C₈ alkyl, -(C₀-C₃ alkyl)-(C₃-C₈ cycloalkyl), -(C₁-C₄ alkyl)-A', or A', wherein the alkyl

groups and the cycloalkyl groups in the definition of R^2 are optionally substituted with hydroxy, -CO2 X^6 , -CONX $^6X^6$, -NX $^6X^6$, -SO_m(C₁-C₆ alkyl), - COA', -COX 6 , CF₃, CN, or 1, 2, or 3 independently selected halo groups;

 R^3 is selected from the group consisting of A', C_1 - C_{10} alkyl, - $(C_1$ - C_6 alkyl)-A', - $(C_1$ - C_6 alkyl)- $(C_3$ - $(C_1$ -

wherein the alkyl groups in the definition of R^3 are optionally substituted with -SO_m(C₁-C₆ alkyl), -CO₂ X3, 1, 2, 3, 4, or 5 independently selected halo groups, or 1, 2, or 3 independently selected -OX³ groups;

X' is O, SO, -NX 2 CO-, -CONX 2 -, -OCO-, -CO $_2$ -, -CX 2 =CX 2 -, -NX 2 CO $_2$ -, -OCONX 2 -, or CC-; R^4 is hydrogen, C_1 - C_6 alkyl, or C_3 - C_7 cycloalkyl, or R^4 taken together with R^3 and the carbon atom to which they are attached form C_5 - C_1 cycloalkyl, C_5 - C_1 cycloalkenyl, a partially saturated or fully saturated 4- to 8-membered ring having 1 to 4 heteroatoms independently selected from the group consisting of oxygen, sulfur, and nitrogen, or a bicyclic ring system consisting of a partially saturated or fully saturated 5- or 6-membered ring, fused to a partially saturated, fully unsaturated, or fully saturated 5- or 6-membered ring, optionally having 1 to 4 heteroatoms independently selected from the group consisting of nitrogen, sulfur, and oxygen;

 X^4 is hydrogen or C_1 - C_6 alkyl, or X^4 is taken together with R^4 and the nitrogen atom to which X^4 is attached and the carbon atom to which R^4 is attached and form a five to seven membered ring; R^6 is a bond or is

$$Z^{1}$$
 (CH₂)a (CH₂)b ;

wherein a and b are each independently O, 1, 2, or 3;

 X^5 and X5a are each independently selected from the group consisting of hydrogen, CF_3 , A^1 , and C_1 - C_6 alkyl optionally substituted with A', OX^2 , - SO, $(C_1$ - C_6 alkyl), - CO_2X^2 , C_3 - C_1 cycloalkyl, - NX^2X^2 , or - $CONX^2X^2$;

or the carbon bearing X^5 or X^{5a} forms one or two alkylene bridges with the nitrogen atom bearing R^7 and R^8 wherein each alkylene bridge contains 1 to 5 carbon atoms, provided that when one alkylene bridge is formed then only one of X^5 or X^{5a} is on the carbon atom and only one of R^7 or R^8 is on the nitrogen atom, and further provided that when two alkylene bridges are formed then X^5 and X^5 a cannot be on the carbon atom and R^7 and R^8 cannot be on the nitrogen atom;

or X⁵ taken together with X^{5a} and the carbon atom to which they are attached form a partially saturated or fully saturated 3- to 7-membered ring, or a partially saturated or fully saturated 4- to 8-membered ring having 1 to 4 heteroatoms independently selected from the group consisting of oxygen, sulfur, and nitrogen;

or X⁵ taken together with X^{5a} and the carbon atom to which they are attached form a bicyclic ring system consisting of a partially saturated or fully saturated 5- or 6-membered ring, optionally having 1

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or 2 heteroatoms independently selected from the group consisting of nitrogen, sulfur, and oxygen, fused to a partially saturated, fully saturated, or fully unsaturated 5- or 6-membered ring, optionally having 1 to 4 heteroatoms independently selected from the group consisting of nitrogen, sulfur, and oxygen;

 $\underline{Z^1}$ is a bond, O, or N-X², provided that when a and b are both O then Z¹ is not N-X2 or O; $\underline{R^7}$ and $\underline{R^8}$ are each independently hydrogen or $\underline{C_1-C_6}$ alkyl optionally independently substituted with A', $\underline{-CO_2-(C_1-C_6)}$ alkyl), $\underline{-SO_m(C_1-C_6)}$ alkyl); 1 to 5 halo groups, 1 to 3 hydroxy groups, 1 to 3 -O-CO($\underline{C_1-C_6}$ alkyl) groups, or 1 to 3 $\underline{C_1-C_6}$ alkoxy groups; or

R' and R⁸ can be taken together to form -(CH₂), L-(CH₂)_r, wherein L is CX^2X^2 , SO_m , or NX^2 ;

R⁹ and R' are each independently selected from the group consisting of hydrogen, fluoro, hydroxy, and C₁-C₅ alkyl optionally independently substituted with 1-5 halo groups;

 R^{11} is selected from the group consisting of C_1 - C_5 alkyl and phenyl optionally substituted with 1-3 substituents each independently selected from the group consisting of C_1 - C_5 alkyl, halo, and C_1 - C_5 alkoxy;

 R^{12} is selected from the group consisting of C_1 - C_5 alkylsulfonyl, C_1 - C_5 alkanoyl, and C_1 - C_5 alkylwherein the alkyl portion is optionally independently substituted by 1-5 halo groups;

A' for each occurrence is independently selected from the group consisting of C_5 - C_7 cycloalkenyl, phenyl, a partially saturated, fully saturated, or fully unsaturated 4- to 8-membered ring optionally having 1 to 4 heteroatoms independently selected from the group consisting of oxygen, sulfur, and nitrogen, and a bicyclic ring system consisting of a partially saturated, fully unsaturated, or fully saturated 5- or 6- membered ring, optionally having 1 to 4 heteroatoms independently selected from the group consisting of nitrogen, sulfur, and oxygen, fused to a partially saturated, fully saturated, or fully unsaturated 5- or 6-membered ring, optionally having 1 to 4 heteroatoms independently selected from the group consisting of nitrogen, sulfur, and 30 oxygen;

A¹ for each occurrence is independently optionally substituted, on one or optionally both rings if A' is a bicyclic ring system, with up to three substituents, each substituent independently selected from the group consisting of F, Cl, Br, I, OCF3, OCF2H, CF3, CH3, OCH3, -OX6, -CONX6X6, -CO2 X6, oxo, C1- C_6 alkyl, nitro, cyano, benzyl, -SO1(C_1 - C_6 alkyl), 1 H-tetrazol-5-yl, phenyl, phenoxy, phenylalkyloxy, halophenyl, methylenedioxy, -NX6X6, -NX6COX6, -SO2NX6X6, -NX6SO2-phenyl, NX6SOX, - $CONX^{11}X^{12}$, -SO2NX $^{11}X^{12}$, -NX6SO2 12 , imidazolyl, thiazolyl, and tetrazolyl, provided that if A' is optionally substituted with methylenedioxy then it can only be substituted with one methylenedioxy; wherein X^{11} is hydrogen or C_1 - C_6 alkyl optionally independently substituted with phenyl, phenoxy, C_1 Cs alkoxycarbonyl, -SO 12 (C_1 - C_6 alkyl), 1 to 5 halo groups, 1 to 3 hydroxy groups, 1 to 3 C_1 - C_6 alkyl, phenyl, thiazolyl, imidazolyl, furyl, or thienyl, provided that when X^{12} is not hydrogen, C_1 - C_6 alkyl, phenyl, thiazolyl, imidazolyl, furyl, or thienyl, provided that when X^{12} is not hydrogen, the X^{12} group is optionally substituted with one to three substituents independently selected from the group consisting of Cl, F, CH_3 , OCH_3 , OCE_3 , and CE_3 .

or X¹¹ and X¹² are taken together to form -(CH₂)_rL¹(CH₂), , wherein L¹ is CX²X², O, SO, or NX²;

r for each occurrence is independently 1, 2, or 3;

 X^2 for each occurrence is independently hydrogen, optionally substituted C_1 - C_6 alkyl, or optionally substituted C_3 - C_7 cycloalkyl, wherein the optionally substituted C_1 - C_6 alkyl and optionally substituted C_3 - C_1 cycloalkyl in the definition of X^2 are optionally independently substituted with - $SO_m(C_1$ - C_6 alkyl), -CO2 X3, 1 to 5 halo groups, or 1-3 OX^3 groups;

X³ for each occurrence is independently hydrogen or C1-C₆ alkyl;

 X^6 for each occurrence is independently hydrogen, optionally substituted C_1 - C_6 alkyl, halogenated C_2 - C_6 alkyl, optionally substituted C_3 - C_7 cycloalkyl, halogenated C_3 - C_7 cycloalkyl, wherein the optionally substituted C_1 - C_6 alkyl and optionally substituted C_3 - C_1 cycloalkyl in the definition of X^6 are optionally independently mono or di-substituted with C_1 - C_4 alkyl, hydroxy, C_1 - C_4 alkoxy, carboxyl, CONH $_2$, - $SO_m(C_1$ - C_6 alkyl), carboxylate (C_1 - C_4 alkyl) ester, or 1 H-tetrazol-5-yl; or when there are two X^6 groups on one atom and both X^6 are independently C_1 - C_6 alkyl, the two C_1 - C_6

alkyl groups may be optionally joined, and together with the atom to which the two X^6 groups are attached, form a 4- to 9- membered ring optionally having oxygen, sulfur, or NX^7 as a ring member, wherein X^7 is hydrogen or C_1 - C_6 alkyl optionally substituted with hydroxy;

m for each occurrence is independently O, 1, or 2; with the provisos that:

 X^6 and X^{12} cannot be hydrogen when attached to CO or SO_2 in the form COX^6 , COX^{12} , SO_2X^6 or SO_2X^{12} ; and

when R⁶ is a bond then L is NX² and each r in the definition -(CH₂), L-(CH₂), is independently 2 or 3.

- 14. (Currently amended) A pharmaceutical composition according to claim 13 wherein said corticotropin releasing factor antagonist is a compound selected from the group consisting of:
- 4-(1-ethyl-propoxy)-3,6-dimethyl-2-(2,4,6-trimethylphenoxy)-pyridine;
- 4-(1-ethyl propoxy)-2,5-dimethyl-6-(2,4,6-trimethyl phenoxy)-pyrimidine;
- [4-(1-ethyl-propoxy)-3,6-dimethyl-pyridin-2-yl]-(2,4,6-trimethylphenyl)-amine;
- 3-{(4-methyl-benzyl)-[3,6-dimethyl-1-(2,4,6-trimethylphonyl)-1-H-pyrazolo[3,4d]pyrimidin-4-yl]-amino}-propan-1-ol;

propyl-ethyl-[3,6-dimethyl-1-(2,4,6-trimethylphenyl)-1-H-pyrazolo[3,4-d]pyrimidin-4-yl]-amine; ethyl-n-propyl-[2,5-dimethyl-7-(2,4,6-trimethylphenyl)-7H-pyrrolo[2,3d]pyrimidin-4-yl]amine; 2-{N-n-butyl-N-[2,5-dimethyl-7-(2,4,6-trimethylphenyl)-7H-pyrrolo[2,3d]pyrimidin-4-yl]amino}-ethanol;

[3,6-dimethyl-1-(2,4,6-trimethylphenyl)-1-H-pyrazolo[3,4,b]pyridin-4-yl]-(1-methoxymethylpropyl)-amine;

4-(1-ethylpropoxy)-2,5-dimethyl-7-(2,4,6-trimethylphenyl)-7H-pyrrolo[2,3b]pyridine;

2,5,6-trimethyl-7-(1-pro-pylbutyl)-4-(2,4,6-trim ethyl-phenoxy)-7H-pyrrolo[2,3-d]pyrimidine;

1-(1-ethyl-propyl)-6-methyl-4-(2,4,6-trimethylphenoxy)-1,3-dihydro-imidazo[4,5c]pyridin-2-one;

1-(1-ethyl-propyl)-4,7-dimethyl-5-(2,4,6-trimethyl-p he noxy)-1,4-dihydro2H-pyrido[3,4-b]pyrazin-3-one;

1-(1-ethyl-pro-pyl)-4,7-dimethyl-5-(2,4,6-trimethyl-p-hen-oxy)-1,2,3,4tetrahydro-pyrido[3,4-

b]pyrazine;

- 1-(1-ethyl-pro-pyl)-7-methyl-2-oxo-5-(2,4,6-trimethyl-p hen oxy)-1,2,3,4-tetrahydro-[1,6]naphthyridine-3-carboxylic-acid isopropyl-ester;
- 1-(1-ethyl-propyl)-7-methyl-5-(2,4,6-trimethyl-phenoxy)-1,4-dihydro-2H-3oxa-1,6-diaza-naphthalene;
- (1-ethyl-propyl)-[5-methyl-3-(2,4,6-trimethyl-phonyl)-pyrazolo[1,5-a]pyrimidin7-yl]-amine;
- 7-(1-ethyl-propoxy)-2,5-dimethyl-3-(2,4,6-trimethyl-phenyl)-pyrazolo[1,5a]pyrimidine;
- 4-(1-ethyl-propoxy)-2,5-dimethyl-7-(2,4,6-trimethyl-phenyl)-5H-pyrrolo[3,2d]pyrimidine;
- 4-(butyl-ethyl-amino)-2,6-dimethyl-8-(2,4,6-trimethyl-phenyl)-5,8-dihydro-6H-pyrido[2,3-d]pyrimidin-7-one;
- 8-(1-ethyl-propoxy)-6-methyl-4-(2,4,6-trimethyl-phenyl)-1,2,3,4-tetrahydropyrido-[2,3-b]pyrazine;
- 4-(1-ethyl-propoxy)-2-methyl-8-(2,4,6-trimethyl-phonyl)-quinoline; (1-ethyl-propyl)-[2-methyl-8-(2,4,6-trimethyl-phonyl)-quinolin-4-yl]-amine;
- (propyl-ethyl)-[2-methyl-8-(2,4,6-trimethyl-phonyl)-5,6,7,8-tetrahydro-pyrido[2,3-d] pyrimidin-4-yl]-amine;
- (1-ethyl-propoxy)-2-methyl-8-(2,4,6-trimethyl-phenyl)-5,6,7,8-tetrahydropyrido[2,3-d]-pyrimidine; 8-(1-hydroxymethyl-propylamino)-6-methyl-4-(2,4,6-trimethyl-phenyl)-3,4-dihydro-1-H-pyrido[2,3-b]pyrazin-2-one;
- 4-(1-hydroxymethyl-propylamino)-2-methyl-8-(2,4,6-trimethyl-phenyl)quinoline;
- 5-(1-hydroxymethyl-propylamino)-7-methyl-1-(2,4,6-trimethyl-phenyl)-1,4dihydro-2H-3-oxa-1,8-diaza-naphthalene;
- [3,6-dimethyl-2-(2,4,6-trimethyl-phenoxy)-pyridin-4-yl]-(1-ethyl-propyl)-amine; cyclopropylmethyl-[3-(2,4-dimethyl-phenyl)-2,5-dimethyl-pyrazolo[1,5a]pyrimidin-7-yl]-propylamine;
- [2,5-dimethyl-3-(2,4-dimethyl-phenyl)-pyrazolo[1,5-a]pyrimidin-7-yl]-(1-ethylpropyl)-amine; 3-[6-(dimethylamino)-3-pyridinyl-2,5-dimethyl-N,N-dipropylpyrazolo[2,3-a] pyrimidin-7-amine; 3-[6-(dimethylamino)-4-methyl-3-pyridinyl]-2,5-dimethyl-N,N-dipropylpyrazolo[2,3-a]pyrimidine-7-amine;
- 3-(2,4-dimethoxyphonyl)-2,5-dimethyl-7-(N-propyl-N-methyloxyethylamino)pyrazolo(2,3-a)pyrimidine;
- 7-(N-diethylamino)-2,5-dimethyl-3-(2-methyl-4-methoxyphenyl-[1,5-a]pyrazolopyrimidine; and 7-(N-(3-cyano-propyl)-N-propy]-amino-2,5,dimethyl-3-(2,4-dimethylphenyl)-[1,5a]-pyrazolopyrimidine.
- 15. (Cancelled) A pharmaceutical composition according to claim 1 wherein said growth hormone secretagogue is a compound of formula IV:

HET
$$R^4$$
 R^6 R^7 R^8 R^8 R^8

or a stereoisomeric mixture thereof, a diastereomerically enriched, diastereomerically pure, enantiomerically enriched, or enantiomerically pure isomer thereof, or a prodrug of such compound, mixture, or isomer thereof, or a pharmaceutically acceptable salt of the compound, mixture, isomer, or prodrug, wherein:

HET is a heterocyclic moiety selected from the group consisting of

$$\begin{array}{c} & & & \\$$

d is 0, 1, or 2;

e is 1 or 2;

f is 0 or 1;

n and w are 0, 1, or 2, provided that n and w cannot both be O at the same time;

Y² is oxygen or sulfur;

A is a divalent radical, wherein the left hand side of the radical as shown below is connected to C" and USERS/DOCS/LA21952/LPAED/4/65y011.DOC/212902 - 40 -

the right hand side of the radical as shown below is connected C', selected from the group consisting of -NR2-CO-NR2-, -NR2-SO2-NR2-, -O-CO-NR2-, -NR2-CO2-, -CO-NR2-CO-, -CO-NR2-C(R9R10O)-, -C(R⁹R¹⁰)-NR²-CO-,-C(R⁹R¹⁰)-C(R⁹R¹⁰)-C(R⁹R¹⁰)-, -SO₂-C(R⁹R¹⁰)-C(R⁹R¹⁰)-C(R⁹R¹⁰)-O-CO-. - $C(R^9R^{10})-O-C(R^9R^{10})-$, $-NR^2-CO-C(R^9R^{10})-$, $-O-CO-C(R^9R^{10})-$, $-C(R^9R^{10})-$, $-C(R^9R^{10})-$ C(R⁹R¹⁰)-CO₂-, -CO-NR²-C(R⁹R¹⁰)-C(R⁹R¹⁰)-CO₂-C(R⁹R¹⁰)-, -C(R⁹R¹⁰)-C(R⁹R¹⁰)-C(R⁹R¹⁰)-C(R⁹R¹⁰)-, -C(R⁹R¹⁰)-C SO₂-NR²-C(R⁹R¹⁰)-C(R⁹R¹⁰)-, -C(R⁹R¹⁰)-C(R⁹R¹⁰)-NR²-CO-, -C(R⁹R¹⁰)-C(R⁹R¹⁰)-O-CO-, -NR²-CO-C(R⁹R¹⁰)-C(R⁹R¹⁰)--NR²-SO₂-C(R⁹R¹⁰)-C(R⁹R¹⁰)--O-CO-C(R⁹R¹⁰) NR^2 -, $-C(R^9R^{10})-C(R^9R^{10})-CO$ - $-C(R^9R^{10})-NR^2-CO_2-C(R^9R^{10})-O-CO-NR^2$, $-C(R^9R^{10})-NR^2-CO-NR^2$ -, $-C(R^9R^{10})-NR^2$ -, $-C(R^9R^{10})-NR^2$ -, $-C(R^9R^{10})-N$ $NR^2-CO_2-C(R^9R^{10})-$, $-NR^2-CO-NR^2-C(R^9R^{10})-$, $-NR^2-SO_2-NR^2-C(R^9R^{10})-$, $-O-CO-NR^2-C(R^9R^{10})-$, $-O-CO-NR^2-C(R^9R^{10}) CO-N=C(R^{11})-NR^2-$, $-CO-NR^2-C(R^{11})=N-$, $-C(R^9R^{10})-NR^{12}-C(R^9R^{10})-$, $-NR^{12}-C(R^9R^{10})-$, $-NR^{12}-C(R^9R^{10}) C(R^9R^{10})-C(R^9R^{10})-C(R^9R^{10})-C(R^9R^{10})-C(R^1R^{10})-C(R$ $-C(R^9R^{10})-NR^{12}-$, $-N=C(R^{11})-NR^2-CO-$, $-C(R^9R^{10})-C(R^9R^{10})-NR^2-SO_{2-}$, $-C(R^9R^{10})-C(R^9R^{10})-SO_{2-}$ NR^2 -, $-C(R^9R^{10})-C(R^9R^{10})-CO_2$ - $-C(R^9R^{10})-SO_2$ - $-C(R^9R^{10})$ - $-C(R^9R^{10})-C(R^9R^{10})-C(R^9R^{10})$ $C(R^9R^{10})-C(R^{10})-C(R^{10})-C(R^{10})-C(R^{10})-C(R^{10})-C(R^{$ and -C(R9R10)-NR2-SO2-NR2-; Q is a covalent bond or CH₂; W is CH or N; X is CR⁹R¹⁰, C=CH₂, or C=O: Y is CR9R10, O, or NR2; Z is C=O, C=S, or SO₂: G¹ is hydrogen, halo, hydroxy, nitro, amino, cyano, phenyl, carboxyl, -CONH₂, -C₁-C₄ alkyl optionally independently substituted with one or more phenyl, one or more halogen, or one or more hydroxy groups, -C₁-C₄ alkoxy optionally independently substituted with one or more phenyl, one or more halogen, or one or more hydroxy groups, -C₁-C₄ alkylthio, phenoxy, -CO₂-(C₁-C₄ alkyl), N,N-di-(C₁-C₄ alkylamino), -C₂-C₆ alkenyl optionally independently substituted with one or more phenyl, one or more halogen, or one or more hydroxy groups, -C2-C6 alkynyl optionally independently substituted with one or more phenyl, one or more halogen, or one or more hydroxy groups, -C₃-C₆ cycloalkyl optionally independently substituted with one or more C₁-C₄ alkyl groups, one or more halogen, or one or more hydroxy groups, -C₁-C₄ alkylamino carbonyl, or di-C₁-C₄ alkylamino) carbonyl; G2 and G³ are each independently selected from the group consisting of hydrogen, halo, hydroxy, -C₁-C₄ alkyl optionally independently substituted with one to three halo groups, and -C₁-C₄ alkoxy optionally independently substituted with one to three halo groups: R^{1} is hydrogen, -CN, -(CH₂)_aNX⁶COX⁶, -(CH₂)_aNX⁶CO(CH₂)-A¹, -(CH₂)_aNX⁶SO₂(CH₂)-A¹, - $(CH_2)_qNX^6SO_2X^6$, $-(CH_2)_qNX^6CONX^6(CH_2)_t-A^1$, $-(CH_2)_qNX^6CONX^6X^6$, $-(CH_2)_qCONX^6X^6$. $(CH_2)_aCONX^6(CH_2)_t-A^1$, $-(CH_2)_aCO_2X^6$, $-(CH_2)_aCO_2(CH_2)_t-A^1$, $-(CH_2)_aOX^6$, $-(CH_2)_aOOX^6$. $(CH_2)_{a}OCO(CH_2)_{t}-A^{1}$, $-(CH_2)_{a}OCONX^{6}(CH_2)_{t}-A^{1}$, $-(CH_2)_{a}OCONX^{6}X^{6}$, $-(CH_2)_{a}COX^{6}$, $-(CH_2)_{a}COX^{6}$ $(CH_2)_qCO(CH_2)_t-A^1$, $-(CH_2)_qNX^6CO_2X^6$, $-(CH_2)_qNX^6SO_2NX^6X^6$, $-(CH_2)_qSO_mX^6$.

 $(CH_2)_qSO_m(CH_2)_t-A^1$, $-C_1-C_{10}$ alkyl, $-(CH_2)_t-A^1$, $-(CH_2)_q-(C_3-C_1$ cycloalkyl), $-(CH_2)_q-Y^1-(C_1-C_6$ alkyl), $-(CH_2)_q-Y^1-(CH_2)_t-A^1$, or $-(CH_2)_q-Y^1-(CH_2)_t-C_1$ cycloalkyl);

wherein the alkyl and cycloalkyl groups in the definition of R^1 are optionally substituted with C_1 - C_4 alkyl, hydroxy, C_1 - C_4 alkoxy, carboxyl, - CONH₂, -SO_m-(C_1 - C_6 alkyl), -CO₂-(C_1 - C_4 alkyl) ester, 1H-tetrazol-5-yl, or 1, 2, or 3 fluoro groups;

Y' is O, SO_m , $-CONX^6$ -, -CH=CH-, -C=C-, $-NX^6CO$ -, $-CONX^6$ -, $-CO_2$ -, $-OCONX^6$ - or -OCO-; q is O, 1, 2, 3, or 4;

t is O, 1, 2, or 3;

said $(CH_2)_q$ group and $(CHA \text{ group in the definition of R' are optionally independently substituted with hydroxy, <math>C_1$ - C_4 alkoxy, carboxyl, -CONH₂, -SO_m,-(C_1 - C_6 alkyl), -CO₂-(C_1 - C_4 alkyl) ester, 1 H-tetrazol-5-yl, 1, 2, or 3 fluoro groups, or 1 or 2 C_1 - C_4 alkyl groups;

 R^{1A} is selected from the group consisting of hydrogen, F, CI, Br, I, C_1 - C_6 alkyl, phenyl-(C_1 - C_3 alkyl), pyridyl-(C_1 - C_3 alkyl), thiazolyl-(C_1 - C_3 alkyl), and thienyl-(C_1 - C_3 alkyl), provided that R^{1A} is not F, CI, Br, or I when a heteroatom is vicinal to C'';

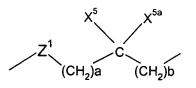
 R^2 is hydrogen, C_1 - C_8 alkyl, -(C_0 - C_3 alkyl)-(C_3 - C_8 cycloalkyl), -(C_1 - C_4 alkyl)-A', or A', wherein the alkyl groups and the cycloalkyl groups in the definition of R^2 are optionally substituted with hydroxy, -CO2 X^6 , -CON X^6X^6 , -N X^6X^6 , -SO_m(C_1 - C_6 alkyl), - COA', -COX⁶, CF₃, CN, or 1, 2, or 3 independently selected halo groups;

 R^3 is selected from the group consisting of A', C_1 - C_{10} alkyl, -(C_1 - C_6 alkyl)-A', - (C_1 - C_6 alkyl)-(C_3 - C_1 cycloalkyl), -(C_1 - C_5 alkyl)-X'-(C_1 - C_5 alkyl)-X'-(C_1 - C_5 alkyl)-X'-(C_1 - C_5 alkyl)-(C_3 - C_1 cycloalkyl);

wherein the alkyl groups in the definition of R^3 are optionally substituted with -SO_m(C₁-C₆ alkyl), -CO2 X^3 , 1, 2, 3, 4, or 5 independently selected halo groups, or 1, 2, or 3 independently selected -OX³ groups;

X' is O, SO_m , $-NX^2CO_-$, $-CONX^2_-$, $-OCO_+$, $-CO_2_-$, $-CX^2_-$ CX², $-NX^2CO_2_-$, $-OCONX^2_-$, or $-C^*C_-$; R⁴ is hydrogen, C_1 - C_6 alkyl, or C_3 - C_7 cycloalkyl, or R⁴ taken together with R³ and the carbon atom to which they are attached form C_5 - C_1 cycloalkyl, C_5 - C_1 cycloalkenyl, a partially saturated or fully saturated 4- to 8-membered ring having 1 to 4 heteroatoms independently selected from the group consisting of oxygen, sulfur, and nitrogen, or a bicyclic ring system consisting of a partially saturated or fully saturated 5- or 6-membered ring, fused to a partially saturated, fully unsaturated, or fully saturated 5- or 6-membered ring, optionally having 1 to 4 heteroatoms independently selected from the group consisting of nitrogen, sulfur, and oxygen;

 X^4 is hydrogen or C_1 - C_6 alkyl, or X^4 is taken together with R^4 and the nitrogen atom to which X^4 is attached and the carbon atom to which R^4 is attached and form a five to seven membered ring; R^6 is a bond or is



wherein a and b are each independently O, 1, 2, or 3;

 X^5 and X5a are each independently selected from the group consisting of hydrogen, CF_3 , A', and C_1 - C_6 alkyl optionally substituted with A', OX^2 , - SO,- $(C_1$ - C_6 alkyl), - CO_2 X2, C_3 - C_7 cycloalkyl, - NX^2X^2 , or - $CONX^2X^2$;

or the carbon bearing X^5 or X^{5a} forms one or two alkylene bridges with the nitrogen atom bearing R^7 and R^8 wherein each alkylene bridge contains 1 to 5 carbon atoms, provided that when one alkylene bridge is formed then only one of X^5 or X^5 a is on the carbon atom and only one of R^7 or R^8 is on the nitrogen atom, and further provided that when two alkylene bridges are formed then X^5 and X^{5a} cannot be on the carbon atom and R^7 and R^8 cannot be on the nitrogen atom;

or X⁵ taken together with X ^{5a} and the carbon atom to which they are attached form a partially saturated or fully saturated 3- to 7-membered ring, or a partially saturated or fully saturated 4- to 8-membered ring having 1 to 4 heteroatoms independently selected from the group consisting of oxygen, sulfur, and nitrogen;

or X^5 taken together with X^{5a} and the carbon atom to which they are attached form a bicyclic ring system consisting of a partially saturated or fully saturated 5- or 6-membered ring, optionally having 1 or 2 heteroatoms independently selected from the group consisting of nitrogen, sulfur, and 30

oxygen, fused to a partially saturated, fully saturated, or fully unsaturated 5- or 6-membered ring, optionally having 1 to 4 heteroatoms independently selected from the group consisting of nitrogen, sulfur, and oxygen;

 Z^1 is a bond, O, or N- X^2 , provided that when a and b are both O then Z' is not N- X^2 or O; R^7 and R^8 are each independently hydrogen or C_1 - C_6 alkyl optionally independently substituted with A', $-CO_2$ - $(C_1$ - C_6 alkyl), $-SO_m(C_1$ - C_6 alkyl), 1 to 5 halo groups, 1 to 3 hydroxy groups, 1 to 3 -O-CO(C_1 - C_{10} alkyl) groups, or 1 to 3 C_1 - C_6 alkoxy groups; or

 R^7 and R^8 can be taken together to form -(CH₂), L-(CH₂), wherein L is CX^2X^2 , SO,, or NX^2 ; R^9 and R^{10} are each independently selected from the group consisting of hydrogen, fluoro, hydroxy, and C₁-C5 alkyl optionally independently substituted with 1-5 halo groups;

 R^{11} is selected from the group consisting of C_1 - C_5 alkyl and phenyl optionally substituted with 1-3 substituents each independently selected from the group consisting of C_1 - C_5 alkyl, halo, and C_1 - C_5 alkoxy;

 R^{12} is selected from the group consisting of C_1 - C_5 alkylsulfonyl, C_1 - C_5 alkanoyl, and C_1 - C_5 alkyl wherein the alkyl portion is optionally independently substituted by 1-5 halo groups;

A¹ for each occurrence is independently selected from the group consisting of C₅-C7 cycloalkenyl, phenyl, a partially saturated, fully saturated, or fully unsaturated 4to 8-membered ring optionally having 1 to 4 heteroatoms independently selected from the group consisting of oxygen, sulfur, and nitrogen, and a bicyclic ring system consisting of a partially saturated, fully unsaturated, or fully saturated 5- or 6 membered ring, optionally having 1 to 4 heteroatoms independently selected from the group consisting of nitrogen, sulfur, and oxygen, fused to a partially saturated, fully saturated, or fully unsaturated 5- or 6-membered ring, optionally having 1 to 4 heteroatoms independently selected

from the group consisting of nitrogen, sulfur, and oxygen;

A¹ for each occurrence is independently optionally substituted, on one or optionally both rings if A' is a bicyclic ring system, with up to three substituents, each substituent independently selected from the group consisting of F, Cl, Br, I, OCF₃, OCF₂H, CF₃, CH₃, OCH₃, $-OX^6$, $-CONX^6X^6$, $-CO_2X^6$, oxo, $C_1^-C_6$ alkyl, nitro, cyano, benzyl, $-SO_m(C_1-C_6$ alkyl), 1 H-tetrazol-5-yl, phenyl, phenoxy, phenylalkyloxy, halophenyl, methylenedioxy, $-NX^6X^6$, $-NX^6COX^6$, $-SO_2NX^6X^1$, $-NX^6SO_2$ -phenyl, $NX^6SO_2X^6$, $-CONX^{11}X^{12}$, $-SO_2NX^{11}X^{12}$, $-NX^6SO_2X^{12}$, $-NX^6COX^{11}X^{12}$, $-NX^6COX^{11}X^{12}$, $-NX^6COX^{12}$, imidazolyl, thiazolyl, and tetrazolyl, provided that if A¹ is optionally substituted with methylenedioxy then it can only be substituted with one methylenedioxy;

wherein X^{11} is hydrogen or C_1 - C_6 alkyl optionally independently substituted with phenyl, phenoxy, C_1 - C_6 alkoxycarbonyl, -SO_M(C_1 - C_6 alkyl), 1 to 5 halo groups, 1 to 3 hydroxy groups, 1 to 3 C_1 - C_{10} alkanoyloxy groups, or 1 to 3 C_1 - C_6 alkoxy groups;

 X^{12} is hydrogen, C_1 - C_6 alkyl, phenyl, thiazolyl, imidazolyl, fury[, or thienyl, provided that when X^{12} is not hydrogen, the X^{12} group is optionally substituted with one to three substituents independently selected from the group consisting of CI, F, CH₃, OCH₃, OCF₃, and CF₃;

or X" and X'^2 are taken together to form -(CH2)r-L¹-(CH₂)_r, wherein L¹ is CX^2X^2 , O, SO_m or NX^2 ; r for each occurrence is independently 1, 2, or 3;

 X^2 for each occurrence is independently hydrogen, optionally substituted C_1 - C_6 alkyl, or optionally substituted C_3 - C_7 cycloalkyl, wherein the optionally substituted C_1 - C_6 alkyl and optionally substituted C_3 - C_1 cycloalkyl in the definition of X^2 are optionally independently substituted with -SO_m(C_1 - C_6 alkyl), -CO2 X^3 , 1 to 5 halo groups, or 1-3 OX 3 groups;

X³ for each occurrence is independently hydrogen or C₁-C₆ alkyl;

 X^6 for each occurrence is independently hydrogen, optionally substituted C_1 - C_6 alkyl, halogenated C_2 - C_6 alkyl, optionally substituted C_3 - C_7 cycloalkyl, halogenated C_3 - C_7 cycloalkyl, wherein the optionally substituted C_1 - C_6 alkyl and optionally substituted C_3 - C_7 cycloalkyl in the definition of X^6 are optionally independently mono-or di-substituted with C_1 - C_4 alkyl, hydroxy, C_1 - C_4 alkoxy, carboxyl, CONH₂, - $SO_m(C_1C_6$ alkyl), carboxylate (C_1 - C_4 alkyl) ester, or 1 H-tetrazol-5-yl; or

when there are two X^6 groups on one atom and both X^6 are independently C_1C_6 alkyl, the two C_1-C_6 alkyl groups may be optionally joined, and together with the atom to which the two X^6 groups are attached, form a 4- to 9- membered ring optionally having oxygen, sulfur, or NX^7 as a ring member, wherein X^7 is hydrogen or C_1-C_6 alkyl optionally substituted with hydroxy;

m for each occurrence is independently O, 1, or 2; with the provisos that:

 X^6 and X'2 cannot be hydrogen when attached to CO or SO_2 in the form COX^6 , COX'^2 , $SO_2 X^6$ or $SO_2 X'^2$; and

when R⁶ is a bond then L is NX² and each r in the definition -(CH₂), L-(CH₂), is independently 2 or 3.

16. (Currently amended) A pharmaceutical composition according to claim 45 ± 4 wherein said growth hormone secretagogue is

2-amino-N-(2-(3a-(R)-benzyl-2-methyl-3-oxo-2,3,3a,4,6,7-hexahydropyrazolo-[4,3-c]pyridin-5-yl)-1-

(R)-benzyloxymethyl-2-oxo-ethyl)isobutyramide;

2-amino-N-(1-(R)-(2,4-difluoro-benzyloxymethyl)-2-oxo-2-(3-oxo-3a(R)-pyridin-2-ylmethyl)-2-(2,2,2-trifluoro-ethyl)-2,3,3a,4,6,7-hexahydro-pyrazolo-[4,3-c]pyridin-5-yl)-ethyl)-2-methyl-propionamide; 2-amino-N-{1(R)-benzyloxymethyl-2-[1,3-dioxo-8a(S)-pyridin-2ylmethyl-2-(2,2,2-trifluoro-ethyl)-hexahydro-imidazo[1,5-a]pyrazin-7-yl]-2-oxoethyl}-2-methyl-propionamide; N-(1(R)-((1,2-dihydro-1-methanesulfonyl-spiro(3H-indole-3,4'-piperidin)-1'-yl)carbonyl)-2-(phenylmethyloxy)ethyl)-2-amino-2-methylpropanamide; or a prodrug of any of these compounds or a pharmaceutically acceptable salt of any of said compounds or said prodrugs.

17. (Cancelled) A pharmaceutical composition according to claim 13 wherein said growth hormone secretagogue is a compound of formula IV:

HET
$$R^4$$
 R^6 R^7 R^8

IV

or a stereoisomeric mixture thereof, a diastereomerically enriched, diastereomerically pure, enantiomerically enriched, or enantiomerically pure isomer thereof, or a prodrug of such compound, mixture, or isomer thereof, or a pharmaceutically acceptable salt of the compound, mixture, isomer, or prodrug, wherein:

HET is a heterocyclic moiety selected from the group consisting of

$$\begin{array}{c} Z \\ X \\ Q \\ R^1 \end{array}$$

$$\begin{array}{c} Z \\ X \\ Q \\ R^1 \end{array}$$

$$\begin{array}{c} Z \\ X \\ Q \\ R^1 \end{array}$$

$$\begin{array}{c} Z \\ X \\ Q \\ R^1 \end{array}$$

$$\begin{array}{c} Z \\ X \\ Q \\ R^1 \end{array}$$

$$\begin{array}{c} Z \\ X \\ Q \\ R^1 \end{array}$$

$$\begin{array}{c} Z \\ X \\ Q \\ R^1 \end{array}$$

$$\begin{array}{c} Z \\ X \\ Q \\ R^1 \end{array}$$

$$\begin{array}{c} Z \\ X \\ Q \\ R^1 \end{array}$$

$$\begin{array}{c} Z \\ X \\ Q \\ R^2 \end{array}$$

$$\begin{array}{c} Z \\ X \\ Q \\ Q \\ Q \\ Q \\ Q \end{array}$$

$$\begin{array}{c} Z \\ X \\ Q \\ Q \\ Q \end{array}$$

$$\begin{array}{c} Z \\ X \\ Q \\ Q \\ Q \end{array}$$

$$\begin{array}{c} Z \\ X \\ Q \\ Q \end{array}$$

$$\begin{array}{c} Z \\ X \\ Q \\ Q \end{array}$$

$$\begin{array}{c} Z \\ X \\ Q \\ Q \end{array}$$

$$\begin{array}{c} Z \\ X \\ Q \end{array}$$

$$\begin{array}{c} Z \\ Z \\ Z \end{array}$$

$$\begin{array}{c} Z \\ Z \end{array}$$

$$\begin{array}{c} Z \\ Z \\ Z \end{array}$$

$$\begin{array}{c} Z$$

d is O, 1, or 2;

e is 1 or 2;

f is O or 1;

n and w are O, 1, or 2, provided that n and w cannot both be O at the same time; Y^2 is oxygen or sulfur;

A is a divalent radical, wherein the left hand side of the radical as shown below is connected to C" and the right hand side of the radical as shown below is connected to C', selected from the group consisting of $-NR^2$ -CO- NR^2 -, $-NR^2$ -SO₂- NR^2 -, -O-CO- NR^2 -, $-NR^2$ -CO₂-, -CO- NR^2 -CO-, -CO- NR^2 -C(R⁹R¹⁰)-, $-C(R^9R^{10})$ -, $-C(R^9R^{10})$ -,

$$\begin{split} &C(R^9R^{10})\text{-, -NR}^2\text{-C}(R^{11})\text{=N-CO--C}(R^9R^{10})\text{-C}(R^9R^{10})\text{-N}(R^{12})\text{-C}(R^9R^{10})\text{-NR}^{12}\text{-, -N=C}(R^1)\text{-NR}^2\text{-CO-, -}\\ &C(R^9R^{10})\text{-C}(R^9R^{10})\text{-NR}^2\text{-SO}_2\text{-, -C}(R^9R^{10})\text{-C}(R^9R^{10})\text{-SO}_2\text{-NR}^2\text{-, -C}(R^9R^{10})\text{-C}(R^9R^{10})\text{-CO}_2\text{-, -C}(R^9R^{10})\text{-CO}_2\text{-, -C}(R^9R^{10})\text{-C}(R^9R^$$

Q is a covalent bond or CH2; W is CH or N;

X is CR⁹R¹⁰, C=CH₂, or C=O; Y is CR⁹R¹⁰, O, or NR²;

Z is C=O, C=S, or SO₂;

 G^1 is hydrogen, halo, hydroxy, nitro, amino, cyano, phenyl, carboxyl, -CONH₂, -C₁-C₄ alkyl optionally independently substituted with one or more phenyl, one or more halogen, or one or more hydroxy groups, -C₁-C₄ alkoxy optionally independently substituted with one or more phenyl, one or more halogen, or one or more hydroxy groups, -C₁-C₄ alkylthio, phenoxy, -CO₂-(C₁-C₄ alkyl), N,N-di-(C₁-C₄ alkylamino), -C₂-C₆ alkenyl optionally independently substituted with one or more phenyl, one or more halogen, or one or more hydroxy groups, -C₂-C₆ alkynyl optionally independently substituted with one or more phenyl, one or more halogen, or one or more hydroxy groups, -C₃-C₆ cycloalkyl optionally independently substituted with one or more C₁-C₄ alkyl groups, one or more halogen, or one or more hydroxy groups, -C₁-C₄ alkylamino carbonyl, or di-C₁-C₄ alkylamino) carbonyl;

G² and G³ are each independently selected from the group consisting of hydrogen, halo, hydroxy, -C₁-C₄ alkyl optionally independently substituted with one to three halo groups, and -C₁-C₄ alkoxy optionally independently substituted with one to three halo groups;

 $R^{1} \text{ is hydrogen, -CN, -}(CH_{2})_{q}NX^{6}COX^{6}, -(CH_{2})_{q}NX^{6}CO(CH_{2})_{t}-A^{1} -(CH_{2})_{q}NX^{6}SO_{2}(CH_{2})_{t}-A^{1}, -(CH_{2})_{q}NX^{6}SO_{2}X^{6}, -(CH_{2})_{q}NX^{6}CONX^{6}(CH_{2})_{t}A^{1}, -(CH_{2})_{q}NX^{6}CONX^{6}X^{6}, -(CH_{2})_{q}CONX^{1}X^{6}, -(CH_{2})_{q}CONX^{1}X^{6}, -(CH_{2})_{q}COX^{6}, -(CH_{2})_{q}COX^{6$

wherein the alkyl and cycloalkyl groups in the definition of R' are optionally substituted with C_1 - C_4 alkyl, hydroxy, C_1 - C_4 alkoxy, carboxyl, - CONH₂, -SO_m (C_1 - C_6 alkyl), -CO₂-(C_1 - C_4 alkyl) ester, 1 H-tetrazol-5-yl, or 1, 2, or 3 fluoro groups;

Y' is O, SO_m , $-CONX^6$ -, -CH=CH-, -C=C-, $-NX^6CO$ -, $-CONX^6$ -, $-CO_2$ -, $-OCONX^6$ - or -OCO-; q is O, 1, 2, 3, or 4; t is O, 1, 2, or 3;

said (CH2)g group and (CHA group in the definition of R' are optionally independently substituted with hydroxy, C_1 - C_4 alkoxy, carboxyl, -CONH₂, -SO, (C_1 - C_6 alkyl), -CO₂-(C_1 - C_4 alkyl) ester, 1 H-tetrazol-5-yl, 1, 2, or 3 fluoro groups, or 1 or 2 C_1 - C_4 alkyl groups;

 R^{1A} is selected from the group consisting of hydrogen, F, CI, Br, I, C_1 - C_6 alkyl, phenyl-(C_1 - C_3 alkyl), pyridyl-(C_1 - C_3 alkyl), thiazolyl-(C_1 - C_3 alkyl), and thienyl-(C_1 - C_3 alkyl), provided that R^{1A} is not F, CI, Br, or I when a heteroatom is vicinal to C'';

 R^2 is hydrogen, C_1 - C_8 alkyl, -(C_0 - C_3 alkyl)-(C_3 - C_8 cycloalkyl), -(C_1 - C_4 alkyl)-A', or A', wherein the alkyl

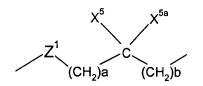
groups and the cycloalkyl groups in the definition of R^2 are optionally substituted with hydroxy, -CO2 X^6 , -CONX $^6X^6$, -NX $^6X^6$, -SO_m(C₁-C₆ alkyl), - COA', -COX 6 , CF₃, CN, or 1, 2, or 3 independently selected halo groups;

 R^3 is selected from the group consisting of A', C_1 - C_{10} alkyl, -(C_1 - C_6 alkyl)-A', - (C_1 - C_6 alkyl)-(C_3 - C_7 cycloalkyl), -(C_1 - C_5 alkyl)-X'-(C_1 - C_5 alkyl)-X'-(C_0 - C_5 alkyl)-A', and -(C_1 - C_5 alkyl)-X'-(C_1 - C_5 alkyl)-(C_3 - C_1 cycloalkyl);

wherein the alkyl groups in the definition of R^3 are optionally substituted with $-SO_m(C_1-C_6 \text{ alkyl})$, $-CO_2 X3$, 1, 2, 3, 4, or 5 independently selected halo groups, or 1, 2, or 3 independently selected $-OX^3$ groups;

X' is O, SO, $-NX^2CO_-$, $-CONX^2_-$, $-OCO_+$, $-CO_2_-$, $-CX^2=CX^2_-$, $-NX^2CO_2_-$, $-OCONX^2_-$, or $-C^2C_-$; $-CX^4$ is hydrogen, $-C_1C_6$ alkyl, or $-C_3C_7$ cycloalkyl, or $-C_3C_7$ cycloalkyl, or $-C_3C_7$ cycloalkyl, a partially saturated or fully saturated 4- to 8-membered ring having 1 to 4 heteroatoms independently selected from the group consisting of oxygen, sulfur, and nitrogen, or a bicyclic ring system consisting of a partially saturated or fully saturated 5- or 6-membered ring, fused to a partially saturated, fully unsaturated, or fully saturated 5- or 6-membered ring, optionally having 1 to 4 heteroatoms independently selected from the group consisting of nitrogen, sulfur, and oxygen;

 X^4 is hydrogen or C_1 - C_6 alkyl, or X^4 is taken together with R^4 and the nitrogen atom to which X^4 is attached and the carbon atom to which R^4 is attached and form a five to seven membered ring; R^6 is a bond or is



wherein a and b are each independently O, 1, 2, or 3;

 X^5 and X5a are each independently selected from the group consisting of hydrogen, CF_3 , A^1 , and C_1 - C_6 alkyl optionally substituted with A', OX^2 , - SO_7 (C_1 - C_6 alkyl), - CO_2 X^2 , C_3 - C_1 cycloalkyl, - NX^2X^2 , or - $CONX^2X^2$;

or the carbon bearing X^5 or X^{5a} forms one or two alkylene bridges with the nitrogen atom bearing R^7 and R^8 wherein each alkylene bridge contains 1 to 5 carbon atoms, provided that when one alkylene bridge is formed then only one of X^5 or X^{5a} is on the carbon atom and only one of R^7 or R^8 is on the nitrogen atom, and further provided that when two alkylene bridges are formed then X^5 and X^5 a cannot be on the carbon atom and R^7 and R^8 cannot be on the nitrogen atom;

or X⁵ taken together with X^{5a} and the carbon atom to which they are attached form a partially saturated or fully saturated 3- to 7-membered ring, or a partially saturated or fully saturated 4- to 8-membered ring having 1 to 4 heteroatoms independently selected from the group consisting of oxygen, sulfur, and nitrogen;

or X⁵ taken together with X^{5a} and the carbon atom to which they are attached form a bicyclic ring system consisting of a partially saturated or fully saturated 5- or 6-membered ring, optionally having 1

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or 2 heteroatoms independently selected from the group consisting of nitrogen, sulfur, and oxygen, fused to a partially saturated, fully saturated, or fully unsaturated 5- or 6-membered ring, optionally having 1 to 4 heteroatoms independently selected from the group consisting of nitrogen, sulfur, and oxygen;

 Z^1 is a bond, O, or N- X^2 , provided that when a and b are both O then Z^1 is not N-X2 or O; R^7 and R^8 are each independently hydrogen or C_1 - C_6 alkyl optionally independently substituted with A', $-CO_2$ - $(C_1$ - C_6 alkyl), $-SO_m(C_1$ - C_6 alkyl); 1 to 5 halo groups, 1 to 3 hydroxy groups, 1 to 3 -O- $CO(C_1$ - C_{10} alkyl) groups, or 1 to 3 C_1 - C_6 alkoxy groups; or

R' and R⁸ can be taken together to form -(CH₂), L-(CH₂)_r, wherein L is CX^2X^2 , SO_m , or NX^2 ; R⁹ and R' are each independently selected from the group consisting of hydrogen, fluoro, hydroxy, and C₁-C₅ alkyl optionally independently substituted with 1-5 halo groups;

 R^{11} is selected from the group consisting of C_1 - C_5 alkyl and phenyl optionally substituted with 1-3 substituents each independently selected from the group consisting of C_1 - C_5 alkyl, halo, and C_1 - C_5 alkoxy;

 R^{12} is selected from the group consisting of C_1 - C_5 alkylsulfonyl, C_1 - C_5 alkanoyl, and C_1 - C_5 alkylwherein the alkyl portion is optionally independently substituted by 1-5 halo groups;

A' for each occurrence is independently selected from the group consisting of C_5 - C_7 cycloalkenyl, phenyl, a partially saturated, fully saturated, or fully unsaturated 4- to 8-membered ring optionally having 1 to 4 heteroatoms independently selected from the group consisting of oxygen, sulfur, and nitrogen, and a bicyclic ring system consisting of a partially saturated, fully unsaturated, or fully saturated 5- or 6- membered ring, optionally having 1 to 4 heteroatoms independently selected from the group consisting of nitrogen, sulfur, and oxygen, fused to a partially saturated, fully saturated, or fully unsaturated 5- or 6-membered ring, optionally having 1 to 4 heteroatoms independently selected from the group consisting of nitrogen, sulfur, and 30 oxygen;

A¹ for each occurrence is independently optionally substituted, on one or optionally both rings if A¹ is a bicyclic ring system, with up to three substituents, each substituent independently selected from the group consisting of F, CI, Br, I, OCF₃, OCF₂H, CF₃, CH₃, OCH₃, $-OX^6$, $-CONX^6X^6$, -CO2X6, oxo, C₁-C₆ alkyl, nitro, cyano, benzyl, $-SO_1(C_1-C_6$ alkyl), 1 H-tetrazol-5-yl, phenyl, phenoxy, phenylalkyloxy, halophenyl, methylenedioxy, $-NX^6X^6$, $-NX^6COX^6$, $-SO_2NX^6X^6$, $-NX^6SO_2$ -phenyl, NX^6SOX , $-CONX^{11}X^{12}$, $-SO_2NX^{11}X^{12}$, $-NX^6SO_2X^{12}$, $-NX^6COX^{11}X^{12}$, $-NX^6COX^{11}X^{12}$, $-NX^6COX^{11}X^{12}$, $-NX^6COX^{12}$, imidazolyl, thiazolyl, and tetrazolyl, provided that if A¹ is optionally substituted with methylenedioxy then it can only be substituted with one methylenedioxy; wherein X^{11} is hydrogen or C_1 -C₆ alkyl optionally independently substituted with phenyl, phenoxy, C_1 Cs alkoxycarbonyl, $-SO_m(C_1-C_6$ alkyl), 1 to 5 halo groups, 1 to 3 hydroxy groups, 1 to 3 C₁-C₁₀ alkanoyloxy groups, or 1 to 3 C₁-C₆ alkoxy groups; X^{12} is hydrogen, C_1 -C₆ alkyl, phenyl, thiazolyl, imidazolyl, furyl, or thienyl, provided that when X^{12} is not hydrogen, the X^{12} group is optionally substituted with one to three substituents independently selected from the group consisting of CI, F, CH₃, OCH₃, OCF₃, and CF₃; or X^{11} and X^{12} are taken together to form -(CH₂)_cL¹-(CH₂), wherein L¹ is CX^2X^2 , O, SO, or NX^2 ;

r for each occurrence is independently 1, 2, or 3;

 X^2 for each occurrence is independently hydrogen, optionally substituted C_1 - C_6 alkyl, or optionally substituted C_3 - C_7 cycloalkyl, wherein the optionally substituted C_1 - C_6 alkyl and optionally substituted C_3 - C_1 cycloalkyl in the definition of X^2 are optionally independently substituted with -SO_m(C_1 - C_6 alkyl), -CO2 X3, 1 to 5 halo groups, or 1-3 OX 3 groups;

X³ for each occurrence is independently hydrogen or C1-C₆ alkyl;

 X^6 for each occurrence is independently hydrogen, optionally substituted C_1 - C_6 alkyl, halogenated C_2 - C_6 alkyl, optionally substituted C_3 - C_7 cycloalkyl, halogenated C_3 - C_7 cycloalkyl, wherein the optionally substituted C_1 - C_6 alkyl and optionally substituted C_3 - C_1 cycloalkyl in the definition of X^6 are optionally independently monoor di-substituted with C_1 - C_4 alkyl, hydroxy, C_1 - C_4 alkoxy, carboxyl, CONH₂, - $SO_m(C_1$ - C_6 alkyl), carboxylate (C_1 - C_4 alkyl) ester, or 1 H-tetrazol-5-yl; or when there are two X^6 groups on one atom and both X^6 are independently C_1 - C_6 alkyl, the two C_1 - C_6 alkyl groups may be optionally joined, and together with the atom to which the two X^6 groups are attached, form a 4- to 9- membered ring optionally having oxygen, sulfur, or NX^7 as a ring member, wherein X^7 is hydrogen or C_1 - C_6 alkyl optionally substituted with hydroxy; m for each occurrence is independently C_1 , or C_1 with the provisos that:

 X^6 and X^{12} cannot be hydrogen when attached to CO or SO_2 in the form COX^6 , COX^{12} , SO_2X^6 or SO_2X^{12} ; and

when R^6 is a bond then L is NX^2 and each r in the definition -(CH_2)_rL-(CH_2)_r is independently 2 or 3.

- 18. (Currently amended) A pharmaceutical composition according to claim 47 13 wherein said growth hormone secretagogue is
- 2-amino-N-(2-(3a-(R)-benzyl-2-methyl-3-oxo-2,3,3a,4,6,7-hexahydro-pyrazolo-[4,3-c]pyridin-5-yl)-1-(R)-benzyloxymethyl-2-oxo-ethyl)-isobutyramide;
- 2-amino-N-(1-(R)-(2,4-difluoro-benzyloxymethyl)-2-oxo-2-(3-oxo-3a-(R)-pyridin-2-ylmethyl)-2-(2,2,2-trifluoro-ethyl)-2,3,3a,4,6,7-hexahydro-pyrazolo-[4,3-c]pyridin-5-yl)-ethyl)-2-methyl-propionamide;
- 2-amino-N-{1(R)-benzyloxymethyl-2-[1,3-dioxo-8a(S)-pyridin-2-ylmethyl-2-(2,2,2-trifluoro-ethyl)-hexahydro-imidazo[1,5-a]pyrazin-7-yl]-2-oxo-ethyl}-2-methyl-propionamide;
- N-(1(R)-((1,2-dihydro-1-methanesulfonyl-spiro(3H-indole-3,4'-piperidin)-1'-yl)carbonyl)-2-(phenylmethyl oxy)ethyl)-2-amino-2-methyl-propanamide; or
- a prodrug of any of these compounds, or a pharmaceutically acceptable salt of any of these compounds or prodrugs.
- 19. (Original) A pharmaceutical composition according to claim 18 wherein said corticotropin releasing factor antagonist is 4-(1-ethyl-propoxy)-3,6-dimethyl-2-(2,4,6-trimethylphenoxy)-pyridine and said growth hormone secretagogue is 2-amino-N-[2-(3a(R)-benzyl-2-methyl-3-oxo-2,3,3a,4,6,7-hexahydro-pyrazolo-[4,3-c]pyridin-5-yl)-1(R)-benzyloxymethyl-2-oxo-ethyl]-isobutyramide.
- 2O. (Original) A pharmaceutical composition according to claim 18 wherein said corticotropin releasing factor antagonist is 4-(1-ethyl- propoxy)-3,6-dimethyl -2-(2,4,6-trimethylphenoxy)-pyridine and said growth hormone secretagogue is 2-amino-N-(1(R)-(2,4-difluoro-benzyloxymethyl)-2-oxo-2-

- (3-oxo-3a(R)-(pyridin-2-ylmethyl)-2-(2,2,2-trifluoro-ethyl)-2,3,3a,4,6,7-hexahydro-pyrazolo-[4,3-c]pyridin-5-yl)-ethyl)-2-methyl-propionamide.
- 21. (Original) A pharmaceutical composition according to claim 18 wherein said corticotropin releasing factor antagonist is (3,6-dimethyl-2-(2,4,6-trimethyl-phenoxy)-pyridin-4-yl)-(1-ethyl- propyl)-a mine and said growth hormone secretagogue is 2-amino-N-[2-(3a(R)-benzyl-2-methyl-3-oxo-2,3,3a,4,6,7-hexahydro-pyrazolo-[4,3-c]pyridin-5-yl)-1(R)-benzyloxymethyl-2-oxo-ethyl]-isobutyramide.
- 22. (Original) A pharmaceutical composition according to claim 18 wherein said corticotropin releasing factor antagonist is (3,6-dimethyl-2-(2,4,6-trimethyl-phenoxy)-pyridin-4-yl)-(1-ethyl-propyl)-amine and said growth hormone secretagogue is 2-15 amino-N-(1(R)-(2,4-difluoro-benzyloxymethyl)-2-oxo-2-(3-oxo-3a(R)-(pyridin-2-ylmethyl)-2-(2,2,2-trifluoro-ethyl)-2,3,3a,4,6,7-hexahydro-pyrazolo-[4,3-c]pyridin-5-yl)-ethyl)-2-methyl-propionamide.
- 23. (Withdrawn) A method for treating or preventing osteoporosis or frailty associated with aging or obesity, said method comprising administering to a human or other animal an amount of a pharmaceutical composition according to claim 1, which is effective in treating or preventing osteoporosis or frailty associated with aging or obesity.
- 24. (Withdrawn) A method for treating or preventing a cardiovascular or heart related disease, said method comprising administering to a human or other animal an amount of a pharmaceutical composition according to claim 1, which is effective in treating or preventing the cardiovascular or heart related disease.
- 25. (Withdrawn) A method according to claim 24 wherein the cardiovascular or heart related disease is hypertension, tachycardia, or congestive heart failure.
- 26. (Withdrawn) A method for accelerating bone fracture repair, attenuating protein catabolic response after a major operation, reducing cachexia and protein loss due to chronic illness, accelerating wound healing, or accelerating the recovery of burn patients or of patients having undergone major surgery, said method comprising administering to a human or other animal an amount of a pharmaceutical composition according to claim 1, which is effective in accelerating bone fracture repair, attenuating protein catabolic response after a major operation, reducing cachexia and protein loss due to chronic illness, accelerating wound healing, or accelerating the recovery of burn patients or of patients having undergone major surgery.
- 27. (Withdrawn) A method for treating or preventing osteoporosis, frailty associated with aging or obesity, cardiovascular or heart related disease, for accelerating bone fracture repair, attenuating protein catabolic response after a major operation, reducing cachexia and protein loss due to chronic illness, accelerating wound healing, or accelerating the recovery of burn patients or of patients having undergone major surgery, said method comprising administering to a human or other animal an amount of a corticotropin releasing factor antagonist and an amount of a growth hormone secretagogue or growth hormone.
- 28. (Withdrawn) The method of claim 27 wherein said corticotropin releasing factor antagonist and said growth hormone secretagogue or growth hormone are administered simultaneously or in a

specifically timed manner.

- 29. (Withdrawn) A kit comprising:
- a. an amount of a corticotropin releasing factor antagonist, in a first unit dosage form;
- b. an amount of a growth hormone secretagogue or growth hormone, in a second unit dosage form; and
 - c. a container.
- 3O. (Currently amended) A kit comprising:
- a. an amount of a corticotropin releasing factor antagonist as defined in claim
 13, in a first unit dosage form;
- b. an amount of a growth hormone secretagogue or growth hormone <u>as</u> <u>defined in Claim 4</u>, in a second unit dosage form; and
 - c. a container.
- 31. (Currently amended) A kit comprising:
- a. an amount of a corticotropin releasing factor antagonist as defined in claim
 14, in a first unit dosage form;
- b. an amount of a growth hormone secretagogue or growth hormone <u>as</u> <u>defined in Claim 4</u>, in a second unit dosage form; and
 - c. a container.
- 32. (Withdrawn) A kit comprising:
- a. an amount of a corticotropin releasing factor antagonist, in a first unit dosage form;
- b. an amount of a growth hormone secretagogue as defined in claim 15, in a second unit dosage form; and
 - c. a container.
- 33. (Currently amended) A kit according to claim 29 30 wherein said corticotropin releasing factor antagonist is 4-(1-ethyl-propoxy)-3,6-dimethyl-2-(2,4,6-trimethylphenoxy)-pyridine or [3,6-dimethyl-2-(2,4,6-dimethyl-phenoxy)-pyridin-4-yl]-(1-ethyl-propyl)-amine, and said growth hormone secretagogue is 2-amino-N-[2-(3a(R)-benzyl-2-methyl-3-oxo-2,3,3a,4,6,7-hexahydro-pyrazolo-[4,3-c]pyridin-5-yl)-1 (R)-benzyloxymethyl-2-oxo-ethyl]-isobutyramide or 2-amino-N-(1-(R)-(2,4-difluoro-benzyloxymethyl)-2-oxo-2-(3-oxo-3a-(R)-pyridin-2-ylmethyl)-2-(2,2,2-trifluoro-ethyl)-2,3,3a,4,6,7-hexahydro-pyrazolo-[4,3-c]pyridin-5-yl)-ethyl)-2-methyl-propionamide.
- 34. (Withdrawn) A kit, comprising
- a. a pharmaceutical composition, comprising an amount of a growth hormone or growth hormone secretagogue;
 - b. a package containing the above composition; and
 - c. a package insert that may be integral with said package;

wherein it is stated on the package insert that the pharmaceutical composition is to be administered simultaneously or in a specifically timed manner with a pharmaceutical composition containing at least one corticotropin releasing factor antagonist.

35. (Withdrawn) A kit, comprising

- a. a pharmaceutical composition, comprising an amount of a corticotropin releasing factor antagonist;
 - b. a package containing the above composition; and
- c. a package insert that may be integral with said package; wherein it is stated on the package insert that the pharmaceutical composition is to be administered simultaneously or in a specifically timed manner with a pharmaceutical composition containing at least one growth hormone or growth hormone secretagogue.